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SURGICAL NEUROLOGY AND BIOLOGY

CHAIRMAN'S ADDRESS

PAUL C. BUCY, M.D.

CHICAGO

> I think my description of the mode of operating and of the anatomy of the part concerned, clear enough to enable any good anatomist, possessing the judgements requisite for a surgeon, to operate with safety. I hope no operator of any other description may even attempt it. It is my most ardent wish that this operation may remain, to the mechanical surgeon, forever incomprehensible. Such have been the bane of the science; intruding themselves into the ranks of the profession, with no other qualification but boldness in undertaking, ignorance of their responsibility and indifference to the lives of their patients. —*Ephraim McDowell*, 1819.

Although cranial surgery was undoubtedly practiced by prehistoric man and by his descendants, little progress was made, and this type of surgery, apart from the relief of demons in individuals suffering from epilepsy and psychoses, was confined to the treatment of wounds and fractures and of other externally visible conditions until the last quarter of the last century. At that time a renaissance of interest in the nervous system was initiated by Fritsch and Hitzig in Germany and by a band of eager spirits in England, which included Jackson, Ferrier and Horsley, to mention only a few. Their studies provided that minimum of information necessary to the beginning of the surgical treatment of those intracranial lesions not visible externally; to permit of the localization of such lesions by deductive reasoning. This beginning was made by Alexander Hughes Bennett, who first so localized an intracranial tumor and persuaded Godlee to operate on it. Sir Victor Horsley, who himself had no small part in the actual experiments which made this development possible, was, however, the first to establish intracranial surgery on a firm basis. Unfortunately, although Horsley's main interest was concerned with the nervous system rather than with surgery, his successors, imitators and pupils were, in the main, general surgeons with little or no interest in the nervous system. They were thus neither interested nor capable of advancing this field of medicine. It is not surprising that at the hands of this disinterested group little or no progress was made in either neurology or neurosurgery. And, as was to be expected, the results of their neurosurgical endeavors were most discouraging. And by the turn of the century the flame of enthusiasm for neurosurgery lit by Horsley in the 1880s was burning very low indeed. At that moment another dynamic figure, fired by the neurologic experiments that he had performed in Kronecker's laboratory and by the ones he had seen in Sherrington's laboratory at Liverpool, appeared in the New World. Harvey Cushing, like Horsley, was not content to deal with the puzzling problems of neurology merely on the basis of existing knowledge. He insisted on personally being in the front line of the attack on neurologic ignorance while at the same time he extended the teachings of Halsted to the field of neurosurgery, masterfully improving its technic as he went. In this same period Charles A. Elsberg in New York and the team of Spiller and Frazier in Philadelphia contributed greatly to the body of knowledge, both technical and diagnostic, in this field. During the six years from the transfer of Cushing from Johns Hopkins to Harvard in 1912 to the close of the war in 1918, intracranial surgery was finally placed on its feet in this country, even though admittedly it toddled rather than walked.

In the ensuing twenty years the members of this branch of the profession have been largely concerned with propagating their kind, with perfecting the technics Cushing gave them and with educating the profession and the public as to their accomplishments. That phase of activity is now largely completed and we seem on the verge of another advance. It is questionable whether we are prepared to make it. We have been so concerned with teaching the young men in this field to execute with reasonable facility the various surgical technics as we now know them that neurosurgeons have been little concerned with seeing that their protégés have had any contact with the basic sciences of anatomy, physiology and pathology, with experimental methods or even with diagnostic neurology. Unbelievable as it may seem, such deficiencies in training are not accidental but often truly deliberate. It would hardly appear necessary to defend the need for the neurosurgeon to be intimately familiar with the structure and function of the part on which he is operating, with the pathologic nature of the lesion which he is treating or to have the ability to recognize clinically not only conditions amenable to the neurosurgical approach but those conditions from which they must be differentiated as well. Yet the chief of one prominent neurosurgical clinic recently said "Why should they know any neurology? They have air and lipiodol, don't they?"

Admittedly in the larger clinical centers it will often be possible for the neurologist and neurosurgeon to work side by side. Such teams, of which that of William G. Spiller and Charles H. Frazier was undoubtedly the most fruitful, have been productive of brilliant results in the past; they may well continue to be so in the future. But such teamwork can be fully productive only when the individuals collaborate on an equal basis. The day has passed when we can tolerate the practice of the days of the barber surgeons, when the

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physician stood by and literally directed the hand of an uneducated, though skilful, technician. Furthermore, there exist many situations in which collaboration between neurologist and neurosurgeon either does not or cannot exist. Even in many of the larger centers the patients of the neurosurgeon are never seen by the neurologist. The diagnosis, the decision as to treatment and the treatment itself all being at the hands of one man, the neurosurgeon. Obviously such a man must be fully trained for his task. But the problem confronting our younger men is often even more difficult, and it is with their training that we are primarily concerned here. They are forced to practice in the smaller cities, often being the only individuals in their community at all familiar with the intricacies of the nervous system. They will have thrust on them an extremely variegated picture of neurologic disease, much of which will not benefit from surgical therapy. If they are to meet their obligations to their patients and their medical colleagues they must be trained in more than the technics of the operating theater.

That he who would attack the various diseases of the nervous system with a knife must be a competent surgeon is obvious and of primary importance. But what does competence imply? Merely facile fingers—a certain technical excellence? Certainly more is required of one in whose hands mankind is forced to trust its brains. A detailed familiarity with anatomy has long been one of the prerequisites for the general surgeon. Yet a study of the structure of the nervous system is all too frequently neglected in training the young neurosurgeon. Surely this defect is one which must be a serious handicap to any surgeon so inadequately trained. But a mere familiarity with the structures and how to cut them is not enough. He must know of their functions. As Harvey Cushing said over a quarter of a century ago, "To successfully cope with the many operative problems offered by the various disorders of the nervous system, a man, after a thorough training in pathology and medicine must study, not only in the neurological clinic but also in the laboratory, the pathology of these afflictions in their histological and—what is more important—in their experimental aspects." Such training is essential if he is to diagnose the condition present, to determine its amenability to surgical treatment and to advise the patient and his family as to the possibilities of the future with any accuracy. Surely no less is to be expected of any man who proposes to pose as a specialist within a limited field.

Although such training and knowledge are obviously of the greatest importance to the neurosurgeon's activities as a practicing physician, I am also concerned in this discussion with the relationship of the neurosurgeon and his training to the advancement of neurologic knowledge. In spite of its vast opportunities to study the structure, function and pathology of the human nervous system, which are also new opportunities so far as biology is concerned, neurosurgery has in the past twenty years contributed much less than it might have. True, neurosurgeons have contributed to our knowledge of the cerebrospinal fluid. They have added much to our knowledge of the nature of cerebral neoplasms, although we still have far to go before we shall have reaped the full benefit from such knowledge. They have extended our understanding of the function of the sympathetic nervous system, although this particular line of progress has been marked by numerous errors and retreats which could have been avoided by fuller anatomic and physiologic information and by thoroughgoing experimental exploration. At the present time it is no exaggeration to state that, with the exception of our very limited knowledge of the visual cortex and the precentral motor fields, neurology and neurosurgery are operating largely on a decorticate or even decerebrate level, so far as knowledge of the nervous system is concerned.

Through the years of inspired experimentation by Sir Charles Sherrington and his pupils we have learned much of the functions of the isolated spinal cord and bulb. Recently Larsell, Dow and their associates have organized our knowledge of the structure and function of the cerebellum to a point where for the first time observations regarding this structure made in the laboratory and in the clinic can be reasonably coordinated and understood. Cannon, Bard, Ranson, Beattie and others have done much to bring order out of chaos in our understanding of the hypothalamus, though much remains there to be done. LeGros Clark and Walker have clearly told us the story of the thalamus and pointed the way toward profitable studies of sensation and the afferent innervation of the cerebral cortex. The structure and function of the primate basal ganglions and cerebral cortex, however, are still represented by a great void in our knowledge, and it is here that the neurosurgeon is presented with his great opportunity; but he must be properly trained and intellectually curious if he is to take advantage of it.

In the elucidation of the structure and function of the human cerebral cortex, animal experimentation in a large measure deserts us. The cerebral cortex of no animal is comparable to that of man. If progress toward solution of its mysteries is not to be longer delayed, the neurosurgeon must be equipped to collaborate in its investigation. The cerebral cortex of the dog or cat is vastly different from that of man and, by comparison, relatively unimportant. Except for a severe impairment of vision, its removal is attended with relatively slight change in such an animal. He still walks and runs, he still eats, he may even propagate his kind. The subhuman primates are of considerably more experimental value, but even here great care must be exercised. The monkey, which is the most widely used, is not man in miniature—and observations made on the monkey, from which one precentral region or even one entire cerebral hemisphere can be removed with little more than a fleeting disturbance in the innervation of the skeletal musculature and general behavior, cannot be transferred uncritically to man. Such observations can serve as little more than guideposts in our study of human cerebral physiology. Only the apes, particularly the chimpanzee, approach anywhere near to man in regard to cerebral structure and function. These animals have but rarely been used for the experimental investigation of cerebral physiology except by such investigators as Horsley, Sherrington and more recently in this country by our vice chairman, Prof. John F. Fulton of Yale University. His far reaching observations have taught and are continuing to teach us much of the structure and function of the cerebral cortex. They are pointing the way to the neurosurgeon who must extend and confirm his observations on man. This is the very real responsibility of the neurosurgeon to biology and to mankind. If he is to meet it he must have an understanding of the fundamentals of neurology. Each neurosurgeon will, of course, have his own inclinations and develop them;

and if he does the field of neurology will be notably enriched. He must have a familiarity with scientific experimental methods. He must appreciate the necessity of multiple observations, the necessity for controls and for thoroughgoing and painstaking investigation and observation. If he has these virtues he will not fall victim to superficial observation, as typified by the now notorious conclusion once drawn by a neurosurgeon that "no appreciable mental effects follow the extirpation of both frontal lobes," a conclusion since refuted by a study which required a 350 page monograph to detail all the manifestations produced by such an amputation.

Fortunately it is not necessary to start "at scratch" with such a study. Foerster and his pupil Penfield have made a solid beginning in studying the effects of electrical cortical stimulation on the human brain. Also animal experimentation has taught us much of the structure and function of the precentral region but by no means all. And, furthermore, many of those facts are yet to be confirmed in man. Animal experimentation has also revealed much as to the visual cortex, and the intensive study by Holmes and others of the patients injured during the World War was similarly if less completely illuminating for man. But there we stop. What is known of the frontal lobes and their function? A beginning has been made but only that. We are still talking in the most general terms. Of fundamental mechanisms we are almost wholly ignorant. The parietal lobe is almost in the same state—our knowledge of the mechanism of sensation is distinctly limited to subcortical levels. And the functions of the human parietal lobe, in the main, have yet to be elucidated. Certainly Fulton and his co-workers have shown its relative unimportance in the sensory field in the subhuman primates. The temporal lobe still remains the complete enigma. Klüver and I have made only a beginning which indicates that it is of the greatest importance to the animal's mental and emotional economy. However, these preliminary experiments on the monkey must be correlated with observations on man himself before their full significance can be appreciated.

It should not be concluded that our ignorance regarding the cerebral cortex is confined to function. Far from it. Our knowledge of the afferent and efferent connections of these areas is also inadequate and often erroneous as well.

Is it to be supposed that the neurosurgeon is to turn anatomist, physiologist and psychologist all at once in order that he may solve these problems? Certainly not. But the patients are often his. The opportunities frequently confront him first; often they are of his own making. He must be sufficiently familiar with the entire field of neurology to recognize the opportunity when it appears, to direct it to the best advantage and to collaborate with his colleagues in its fullest utilization. When such collaboration is attained, progress will be made.

Those surgeons who have spent their lives in developing the technic of neurosurgery to its present high level cannot be reproached for their failure to solve these problems. But they must see to it that their successors are so trained that they will be competent to do so. And the remainder of the medical profession, be they administrators of medical organizations and institutions or clinical colleagues in related fields, must place no handicaps in their way to prevent their doing so. It is hoped that they will lend positive aid toward the realization of the ideals herein proposed.

University of Chicago Clinics.

POSTARSPHENAMINE JAUNDICE

APPARENTLY DUE TO OBSTRUCTION OF INTRAHEPATIC BILIARY TRACT

FRANKLIN M. HANGER JR., M.D.
AND
ALEXANDER B. GUTMAN, M.D.
NEW YORK

Jaundice following administration of arsphenamine ("arsphenamine hepatitis") is usually ascribed to injury of the liver parenchyma. It has been possible in cases terminating fatally to confirm the hepatogenous character of the jaundice by histologic studies, which show marked degenerative changes in the hepatic lobule.[1] In patients with nonfatal jaundice similar though less advanced parenchymal damage is generally assumed to be present and has been demonstrated in a few instances.[2]

In the course of recent studies employing the serum phosphatase determination and the cephalin flocculation test to differentiate obstructive from hepatogenous jaundice,[3] we investigated patients with postarsphenamine jaundice and found as anticipated that the icterus in most instances was of the hepatogenous type. However, results indicative of obstructive jaundice were obtained in some patients, suggesting that icterus following administration of arsphenamine is not always due to liver parenchymal injury but in certain instances is due to obstructive processes within the biliary tract (Hanger[3]). This distinction in physiologic mechanisms has practical implications bearing directly on the question of the proper approach to treatment.

We have summarized in table 1 twelve cases of postarsphenamine jaundice in which evidence of an obstructive reaction to arsenicals was obtained. The clinical picture so strongly suggested occlusion of the common bile duct that four patients were subjected to exploratory operations. In each instance the extrahepatic biliary tract proved to be patent, but biopsy specimens of the liver revealed marked bile stasis in the finer biliary radicles.

The clinical, chemical and pathologic features of the cases in which intrahepatic obstruction developed are so distinctive that they seem to constitute a discrete disease pattern. The characteristics of this syndrome are illustrated by the three case histories which follow:

REPORT OF CASES

CASE 1.—A white woman aged 51 was treated at the Vanderbilt Clinic for syphilis disclosed by a routine blood Wassermann test. It was stated that no primary or secondary lesions existed; symptoms of tertiary syphilis or neurosyphilis were absent although the spinal fluid gave a positive Wassermann reaction. She received a total of 3.5 Gm. of bismuth subsalicylate from April 17 to May 8, 1939, with no reaction.

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TABLE 1.—*Summary of Data in Twelve Cases of Postarsphenamine Jaundice Apparently Due to Obstruction of the Intrahepatic Biliary Tract*

No. Sex Age Race	State of Syphilis	Therapy and Reactions	Date	Serum: Bilirubin Mg./100 Cc.	Serum: Phosphatase, Bodansky Units/100 Cc.	Serum: Cholesterol, Mg./100 Cc.	Serum: Cephalin Flocculation	Bile in Stools	Bile in Urine	Total Duration of Jaundice in Months	Course in Hospital
1 ♀ 51 White	Neurosyphilis (asymptomatic)	Jaundice developed after third injection of arsphenamine (details in text)	5/31/39 6/12/39 6/16/39 6/22/39 6/26/39 6/29/39	5.3 13.6 16.6 15.6 13.7 12.9	19.5 42.7 41.6 33.9 25.1 25.0	204 ... 642 1,120 1,100 1,310	± 0 0	Clay colored for weeks	++	3½	Details in text
2 ♂ 43 White	Latent	Jaundice developed after second injection of neoarsphenamine (details in text)	7/29/39 8/ 7/39 8/15/39 8/22/39 8/31/39	16.0 16.5 13.0 6.6 3.6	10.0 9.0 10.0 9.3 8.4	165 203 219	0	Gray or light brown	++++	6	Details in text
3 ♂ 29 White	Neurosyphilis (asymptomatic)	Jaundice developed after second injection of neoarsphenamine (details in text)	5/20/38 6/ 1/38 6/14/38 6/21/38 7/ 6/38	17.0 15.0 12.5 9.4 2.0	17.6 13.8 11.6 11.8	580 487 488	0 0	Tan	+++	2½	Details in text
4 ♀ 36 Negro	Latent	Bismuth weekly June '37-April '38, no reaction; 4/22/38, bismuth and first neoarsphenamine (0.6 Gm.), no reaction; within 8 hours after second neoarsphenamine (0.6 Gm.). 4/29/38, chills and vomiting, then malaise, weakness; one week later jaundice, itching, light stools, loss of weight	7/26/38 8/ 4/38 9/ 1/38 9/13/38 9/27/38 10/19/38 12/ 9/38	10.4 8.3 15.0 11.7 9.4 5.9 2.0	12.7 18.5 20.1 13.9	254 235	 0	Intermittently tan and clay colored for months	++	7	Intractable itching persisted and was the presenting symptom; fever 99-100 F. for 6 weeks, no gastrointestinal symptoms except anorexia; complete recovery
5 ♀ 22 White	Secondary (rash)	Bismuth May 2, 7, 15, 1935, no reaction; first neoarsphenamine (0.3 Gm.) 5/10/35, no reaction; second arsphenamine (0.3 Gm.) 5/18/35; several hours later, chills, fever, malaise; three days later dermatitis, fever, vomiting; then facial edema, jaundice, itching, light stools; third neoarsphenamine 6/1/35; that night, acute exacerbation	6/ 2/35 6/10/35 6/18/35	11.0 7.5 4.8	... 45.0 43.7	... 476 472	..	Tan	+	1	Rapid subsidence of all symptoms but jaundice; complete recovery
6 ♀ 33 Negro	Tertiary (syphilid)	Bismuth weekly two months, no reaction; first arsphenamine (0.1 Gm.) 3/24/36, questionable reaction; second arsphenamine (0.15 Gm.) 4/1/36; that night chill, fever, vomiting, malaise; next day rash, conjunctivitis, facial edema; then joint pains, diarrhea; after four days jaundice	5/10/36 5/18/36 6/ 4/36 6/28/36	6.0 11.0 6.8 2.0	.... 15.8	...	..	Tan	+	2¾	Rapid subsidence of symptoms except cutaneous lesions, which cleared after 2 weeks, and jaundice, which persisted; complete recovery
7 ♂ 35 Chinese	Syphilitic?	First neoarsphenamine (0.3 Gm.) 3/9/39, no reaction; first bismuth (0.1 Gm.) 3/14/39, no reaction; second neoarsphenamine (0.4 Gm.) 3/18/39, no immediate reaction; that night chills, headache, malaise; neoarsphenamine and bismuth discontinued, then bismuth given twice weekly; jaundice noted in about two weeks after second neoarsphenamine	7/24/39 7/28/39 8/18/39 9/ 6/39 10/ 4/39 10/25/39 11/ 7/39 11/14/39 11/25/39 12/11/39 12/26/30 1/ 9/40 1/22/40	6.5 6.5 4.7 4.0 10.7 5.0 15.0 7.5 6.1 4.0 5.0 8.3 19.0	16.7 14.9 24.7 18.1 25.3 32.5 34.8 35.4 33.7 35.2 26.6 59.2 38.4	159 ... 253 313 357 755 1,250 1,400 1,650 2,400 2,800 3,100 3,050	0 0 0 0 0 0 0 0 0	Intermittently tan and clay colored for months	++++	>7	Jaundice, itching, weight loss the presenting symptoms for months; exploratory operation 8/2/39, no obstruction of common duct found (details in text); transient improvement postoperatively; then recurrence of painless afebrile jaundice due to postoperative adhesions; (exploratory operation 2/6/40)
8 ♂ 36 White	Latent	Bismuth weekly 3 months, no reaction; first arsphenamine (0.1 Gm.) 4/1/36, no reaction; second arsphenamine 4/8/36 (0.2 Gm.), four hours later conjunctivitis; third arsphenamine (0.3 Gm.) 4/15/36, several hours later itching rash on hands; next day nausea, vomiting, jaundice	4/18/36 4/22/36 4/27/36 5/ 8/36 5/15/36	5.6 8.3 8.3 4.3 3.0	.... 24.6 17.1 10.4	...	..	Acholic two weeks then tan	++	1½	Rapid subsidence of symptoms except jaundice; complete recovery
9 ♂ 19 Negro	Latent	One preliminary bismuth injection, no reaction; first arsphenamine 2/14/38, local reaction only; second arsphenamine 2/21/38, after 2 hours malaise, fever, itching; third arsphenamine 3/2/38, after 1 hour vomiting, then fever, conjunctivitis, arthralgia, weakness; then jaundice	3/ 9/38 3/18/38 3/22/38	7.0 3.2 2.2	12.2 .... 14.3	213 325	±	Brown	+++	¾	Rapid subsidence of symptoms except jaundice and persistent temperature of 100 F.; complete recovery

TABLE 1.—*Summary of Data in Twelve Cases of Postarsphenamine Jaundice Apparently Due to Obstruction of the Intrahepatic Biliary Tract—Continued*

No. Sex Age Race	State of Syphilis	Therapy and Reactions	Date	Serum: Bilirubin Mg./100 Cc.	Serum: Phosphatase, Bodansky Units/100 Cc.	Serum: Cholesterol, Mg./100 Cc.	Serum: Cephalin Flocculation	Bile in Stools	Bile in Urine	Total Duration of Jaundice in Months	Course in Hospital
10 ♀ 24 Negro	Latent	Therapy started 3/7/39, bismuth and 0.15 Gm. arsphenamine; anorexia 2 days, sensitive gums; 3/13/39, bismuth and second arsphenamine (0.15 Gm.), later vomiting and questionable jaundice; 3/20/39, bismuth and third arsphenamine (0.2 Gm.), that night chills, fever, vomiting; then diarrhea, abdominal pain, light stools, arthralgia; after 3 days, jaundice, itch	3/27/39 4/ 3/39	7.9 11.5	10.8 20.4	177 347	++++ ++	Gray one week	++	>1½	Gradual subsidence of acute symptoms, persistent jaundice and intractable itching presenting complaints; last seen May 1939, still icteric
11 ♂ 24 Negro	Latent	Received 5 weekly bismuth injections beginning 8/11/33, no reaction; also arsphenamine 0.15 Gm. 8/12/33, 0.25 Gm. 8/17/33, 0.25 Gm. 8/24/33 and 0.2 Gm. 9/5/33; several hours after second arsphenamine, weakness, vomiting, dizziness, feverish; exacerbation of these symptoms with rash on shoulders, itching several hours after third injection; after fourth injection, same plus marked jaundice, diarrhea, clay-colored stools, crampy abdominal pains	9/27/33 10/14/33 11/ 2/33 11/14/33 11/27/33	21.4 16.2 17.9 8.3 9.1	.... 	... 250 	.. 	Clay colored one month	++++	>2½	All acute symptoms soon subsided, jaundice and intractable pruritus persisting; explored 11/3/33, no obstruction of common duct found (details in text); complete recovery
12 ♂ 23 Puerto Rican	Primary	Received 0.2 Gm. arsphenamine and bismuth 1/2/40; slight reaction; 1/4/40, 0.2 Gm. arsphenamine; 1/12/40, 0.3 Gm. arsphenamine and bismuth; 1/16/40, 0.4 Gm. arsphenamine and bismuth; several hours after second and and third injections chill, fever, malaise, nausea; after fourth injection, same with vomiting, abdominal pain, then jaundice with dark urine, light stools, slight itching	1/26/40 1/31/40 2/ 5/40 1/13/40	7.5 15.0 10.5 7.5	26.9 41.9 30.0 22.6	268 411 390 480	0 0 0 0	Tan two weeks then brown	+++	>1	Acute symptoms soon subsided, jaundice and itching persisted; still under observation

May 15 she was given 0.1 Gm. of arsphenamine intravenously, with no reaction. May 22 she received a second injection of 0.15 Gm. of arsphenamine, with no immediate reaction. Six hours later, however, she had a shaking chill and throughout that night she suffered alternate chills and fever, without nausea or vomiting. The next morning she complained of anorexia, drowsiness and weakness but could resume her work as laundress. Several days later she noted transient dark urine and itching of the skin but was not aware of icterus or of acholic stools. She said nothing of these symptoms on returning to the clinic May 29 and received a third injection of 0.2 Gm. of arsphenamine. There was no immediate reaction but a half hour later she had a shaking chill, became nauseated, dizzy and weak and complained of generalized muscle aches. Icteric scleras were noted. There was no abdominal pain at the onset or throughout the course of her illness. She gave no history of gallbladder disease or antecedent jaundice; there was no preceding infection of the upper respiratory tract or dietary indiscretion. There was no history of allergy.

The patient was admitted at once to the Presbyterian Hospital acutely ill and mentally confused, with a temperature of 104 F., pulse rate of 100 and normal blood pressure. Jaundice was marked. An erythematous rash was present on the forearms. The only syphilitic stigmas found were typical Argyll Robertson pupils. The liver and spleen were not enlarged or tender. The hemoglobin and red cell count were normal; the white cell count was 16,600 with 93 per cent polymorphonuclear cells. The sedimentation rate was 45 mm. in one hour. The urine contained bile and albumin (2 plus). The stools were clay colored.

The patient was placed on a high carbohydrate, low fat diet. The fever subsided in four days as did the other symptoms except pruritus, which was the most distressing complaint. The stools remained clay colored for weeks, intermittently showing occult blood. Chemical examination of the blood (table 1) revealed increasing serum bilirubin levels for three weeks (reaching 16.6 mg. per hundred cubic centimeters), associated with serum phosphatase values as high as 42.7 Bodansky units per hundred cubic centimeters, and consistently negative results with the cephalin flocculation test. The serum cholesterol level, which was normal at the outset, rose to over 1,000 mg. per hundred cubic centimeters one month after the onset of jaundice. The hippuric acid test yielded a value of 2.3 Gm. (slightly below the normal minimum value) after three weeks of intense jaundice. Duodenal drainage on several occasions failed to show bile. Roentgenograms of the gallbladder were equivocal as regards the presence of radiopaque stones.

Despite the close correlation with arsenical administration, the clinical and chemical picture was so typical of obstructive jaundice that surgical intervention was contemplated. However, the serum bilirubin and phosphatase levels began to fall about one month after the onset of jaundice, so that conservative management was continued. Slow improvement was noted until the jaundice finally cleared after three and one-half months.

CASE 2.—A previously healthy white man aged 43 consulted his family physician in March 1939 for difficulty in vision. A positive Wassermann reaction was discovered; it was stated that primary and secondary lesions were absent. His physician gave an intravenous injection (probably neoarsphenamine, dosage not known), without untoward reaction. One week later a second intravenous injection was given, with no immediate reaction. But some ten hours later he had a shaking chill lasting about two hours. There was no feverishness and no gastrointestinal or cutaneous reaction. Jaundice appeared on the second day and rapidly became more intense. This was associated with distressing itching and with some

anorexia but no other complaints. About this time the urine became dark and the stools gray. After four weeks there was some darkening in the color of the stools, associated with transient lessening in the intensity of jaundice. He lost 30 pounds (14 Kg.) in the nine week period prior to hospitalization. During this time he was on a high carbohydrate, low fat diet. On admission to the Presbyterian Hospital July 28 the presenting symptoms were intense jaundice and obvious weight loss; the chief complaint was intractable pruritus. The temperature, pulse and blood pressure were normal. The liver edge was palpable 6 cm. below the costal margin and was very firm but not tender. The spleen could not be felt. There was no evidence of cardiovascular syphilis or neurosyphilis. The erythrocyte, hemoglobin and leukocyte content of the blood were all within normal limits. The urine contained bile, a trace of albumin and a few granular casts. The stools were greenish gray but gave a positive reaction to a Schmidt test for bile pigment. Roentgenograms of the gallbladder were negative for radiopaque stones.

The patient was maintained on a high carbohydrate, low fat regimen, also receiving 15 per cent dextrose solution intravenously at frequent intervals. His condition remained unchanged: afebrile, with painless jaundice of undiminished intensity and intractable pruritus. The serum bilirubin continued at a level of about 16 mg. per hundred cubic centimeters, the serum phosphatase fluctuated around 10 Bodansky units per hundred cubic centimeters, and the cephalin flocculation test gave consistently negative results (table 1). August 7, after almost five months of jaundice, an exploratory operation for obstruction of the common bile duct was performed. The common duct was patent and not dilated. A punch biopsy specimen of the liver was obtained (data will be given later). The pathologic diagnosis was chronic cholecystitis, chronic cystic lymphadenitis and cholangitis.

About a week after operation, the jaundice and itching began to diminish and thereafter convalescence was rapid. The stools began to show more bile pigment two weeks after operation and continued to be brown. He was discharged August 31, still slightly icteric, the total duration of jaundice in this instance being about six months.

CASE 3.—A Syrian aged 29 consulted his family physician in March 1938 for care of acute tonsillitis, also requesting a blood Wassermann test, which was positive. It was stated that primary and secondary lesions were absent. April 12, having recovered from his sore throat, he was given 0.45 Gm. of neoarsphenamine. There was no immediate reaction, but several hours later transient weakness and profuse perspiration developed. April 19 the patient received a second intravenous injection of 0.45 Gm. of neoarsphenamine, with no immediate reaction. Four hours later he had a weak spell with a shaking chill, vomited and went to bed (where he remained until hospitalized). The next day fever, nausea and vomiting developed, and jaundice was noted by his physician. The eyes became puffy and red, his "whole body was swollen," and there was moderate diffuse discomfort in the lower part of the abdomen. These symptoms soon subsided, but anorexia persisted and the jaundice deepened. The urine was very dark and the stools light colored; itching appeared and grew steadily worse. Vague muscle pains were noted, particularly marked in the legs. There was no diarrhea at any time. He gave no history of previous antisyphilitic therapy; there was no antecedent jaundice or dietary indiscretion and nothing to suggest gallbladder disease; no history of allergy was given.

When admitted to the Presbyterian Hospital May 19, one month after onset, he was deeply jaundiced and complained chiefly of itching. The temperature was 100 F.; the pulse, respirations and blood pressure were normal. The left pupil was irregular and reacted sluggishly to light and in accommodation (subsequent lumbar puncture showed neurosyphilis); the reflexes were intact. There was no clinical evidence of cardiovascular syphilis. The liver edge was palpable two fingerbreadths below the costal margin but not tender; the spleen was just palpable. The hemoglobin level was 13 Gm. per hundred cubic centimeters; erythrocytes numbered 3,700,000 and leukocytes 7,700, of which 68 per cent were neutrophils, 19 per cent lymphocytes, 4 per cent monocytes, 1 per cent basophils, 3 per cent myelocytes and 5 per cent eosinophils. The platelets numbered 357,000. Reticulocytosis with the count varying from 6 to 18 per cent was noted during the first two weeks. The red cell fragility in saline solution was normal. The erythrocyte sedimentation rate was 113 mm. in one hour. The urine contained bile but no albumin. The stools were light tan and gave negative mercuric chloride reactions for bile. X-ray examinations showed no radiopaque stones in the gallbladder. Duodenal drainage yielded no B bile and no cholesterol or calcium bilirubinate crystals.

The patient was placed on a high carbohydrate, low fat regimen, with forced fluids, vitamin B_1 given intravenously and liver extract intramuscularly. He continued to have a temperature of 100 F., at first consistently then intermittently, throughout his eight week stay in the hospital. During this period, itching remained the presenting complaint, gastrointestinal symptoms being minimal. The stools remained light in color and gave negative results in mercuric chloride tests for bile for the first six weeks. The erythrocyte sedimentation rate remained elevated up to the time of discharge, when it was 53 mm. in one hour. The eosinophilia persisted, but the reticulocytes and myelocytes disappeared after one month. Chemical studies of the blood (table 1) showed serum bilirubin values as high as 17 mg. per hundred cubic centimeters on admission, with a very gradual decline to the slight elevation present at discharge. The serum phosphatase was definitely increased; repeated cephalin flocculation tests gave negative results. The serum cholesterol values were elevated. A moderate and persistent increase in serum globulin (3.1 per cent) was noted. A hippuric acid test May 24, after more than a month of jaundice and at a time when bilirubinemia was very marked, yielded 2.2 Gm., expressed as benzoic acid.

The patient was discharged July 12, free of symptoms, after some two and one-half months of jaundice. His subsequent course has been uneventful.

CLINICAL CHARACTERISTICS OF POSTARSPHENAMINE JAUNDICE APPARENTLY DUE TO OBSTRUCTION OF THE INTRAHEPATIC BILIARY TRACT

In every case included in table 1 jaundice developed during the first course of treatment with intravenous arsenicals, irrespective of whether or not this was preceded or accompanied by bismuth therapy. With few equivocal exceptions, the first intravenous injection was without incident, but reactions of the type under consideration invariably occurred after the second or third intravenous injection of either arsphenamine or neoarsphenamine, in moderate or small dosage. There was nothing else of etiologic significance in the antecedents of most patients: none had been jaundiced before or had had definite symptoms of cholecystitis or cholelithiasis, none admitted dietary indiscretion preceding the onset of jaundice, and none had previously received arsenicals. Patients 3, 8 and 11 had mild infections of the upper respiratory tract shortly before or during their course of treatment. In only one instance (case 9) was there any swelling at the site of injection, and in none was there any immediate, "nitritoid" reaction to suggest errors in the technic of administration or in the substance administered. Patient 11 gave a definite history of allergy; patient 8 gave an equivocal allergic history. In case 7 cholecystectomy two months prior to the appearance of jaundice suggested stricture of the common bile duct as the cause of icterus, but this possibility was excluded by exploration. No correlation with age, sex, race or stage of syphilis could be made out; in at least one instance (case 7) the diagnosis of syphilis was open to doubt because of repeatedly negative Wassermann tests after little treatment.

The reaction in this group of patients was of the delayed type, the usual interval between injection and the appearance of symptoms being from two to ten hours. In those subjects who had symptoms after the second injection but received further treatment never-

theless, the reaction came on more rapidly (within an hour in cases 1 and 9) and more violently. The onset of symptoms in most patients was acute, characteristically initiated by shaking chills and fever with malaise, headache and vertigo and followed after a variable period by anorexia, nausea and vomiting. Some patients did not have chills, the reaction beginning with a gastro-intestinal upset, or as "conjunctivitis" with chemosis, or as dermatitis. A transitory morbilliform or scarlatiniform eruption appeared early on the upper extremities and trunk in six cases, subsequently becoming more extensive in several instances. Diffuse muscle pains and fleeting arthralgias were severe enough in four cases to constitute a major early complaint. Diarrhea, crampy abdominal pains and edema of the face or extremities developed in the first days of illness in several instances.

Jaundice did not appear until one or more days after the onset of symptoms, some patients (particularly Negroes) failing to note it for periods exceeding a week. Cholouria, acholic or hypocholic stools and itching were observed generally at about the time icterus appeared. With the persistence of jaundice and gastrointestinal symptoms (notably anorexia), marked asthenia and considerable weight loss developed as in cases 2 and 4, in which over 30 pounds was lost in the first two months of illness. Marked dehydration in cases 5 and 6 resulted from fluid loss through vomiting, diarrhea and diaphoresis. Enlargement of the liver with extension from 3 to 6 cm. below the costal margin was noted in four patients, associated with slight splenic enlargement in patients 3 and 5. A moderate hypochromic anemia was present in cases 3 and 5. Initial leukocyte counts ranging from 19,000 to 12,500 with 93 per cent neutrophils were observed in acutely ill, febrile patients (patients 1, 5, 6). In cases 3, 10 and 11 there was eosinophilia with a level of 5 to 12 per cent; in case 9 the eosinophilia reached a level of 21 per cent and, in case 12, 50 per cent. The blood in case 3 showed myelocytes ranging

TABLE 2.—*Summary of Data in Eight Cases of Postarsphenamine Jaundice; Typical of the Usual Picture (Consistent with Hepatitis)*

No. Sex Age Race	State of Syphilis	Therapy and Reactions	Date	Serum: Bilirubin Mg./100 Cc.	Serum: Phosphatase, Bodansky Units/100 Cc.	Serum: Cholesterol, Mg./100 Cc.	Serum: Cephalin Flocculation	Bile in Stools	Bile in Urine	Total Duration of Jaundice in Months	Course in Hospital
13 ♀ 35 Negro	Latent (syphilitic?)	Six weekly intravenous injections (probably neoarsphenamine) Feb.-March 1938, no reactions; in May 1938, two months after last injection, noted painless jaundice, anorexia, light stools, then diarrhea; no preceding cold, etc.	6/ 3/38 6/13/38 6/27/38 7/ 5/38	13.0 9.4 5.0 4.3	6.9 8.7 8.9 8.6	150 94 69 74	..... +++	Brown	+	2	Fever (to 100 F.) for 3 weeks, mild gastrointestinal symptoms; little itching; hippuric acid test, 0.83 Gm. excreted; complete recovery
14 ♀ 43 White	Latent (syphilitic?)	Intravenous specific therapy 10 years before (1927); no symptoms referable to syphilis, negative Wassermann in 1937 but given silver arsphenamine (total 2.1 Gm.) May-July 1937, no reactions; 11/24/37, 4½ months after last injection, jaundice, aches, anorexia; no preceding cold, etc.	12/ 3/37 12/15/37 12/21/37	11.7 10.1 9.4	7.3 5.4	250 ...	..... ++++	Clay colored or tan first weeks	+	1½	Afebrile, no marked gastrointestinal symptoms, no pain or itching; complete recovery
15 ♂ 46 White	Latent	Specific treatment 4 years (6 courses arsphenamine, 9 courses bismuth compound) beginning 1935; while under treatment June 1939, jaundice, nausea, asthenia; recovery but recurrence of jaundice after 1 arsphenamine injection Dec. 1939	12/ 8/39 12/22/39	7.0 2.0	7.4 6.4	... 188	+++	Brown	++	½	Malaise, no itching; complete recovery
16 ♂ 42 Negro	Tertiary (cardiovascular)	Twelve bismuth injections, then started arsphenamine June 1937; discontinued after 4 intravenous injections because of abdominal distention, vomiting, diarrhea; several weeks after last injection, jaundice, asthenia, light stools; no preceding cold, etc.	7/24/37 7/27/37 7/29/37 8/ 2/37	15.1 7.5 4.8 2.9	... 4.1	... 	..... ++++	Light brown	++	1½	Afebrile; gastrointestinal symptoms 3 weeks, rapid decrease in jaundice, no itching; complete recovery
17 ♀ 25 Negro	Latent	Beginning March 1939, 3 bismuth then 9 arsphenamine injections, no reactions; after tenth injection, vomiting, weakness; three days after eleventh injection (6/2/39), jaundice, vomiting; no preceding cold; (pregnant, 4th month, March)	6/ 8/39	17.0	14.5	183	+++	Brown	++	1½	Pregnancy, 7th month premature labor; jaundice asymptomatic, no fever; complete recovery
18 ♂ 46 White	Tertiary (cardiovascular)	Intermittent intravenous specific therapy 1920-1937, no reactions; caught cold while receiving silver arsphenamine June 1937, jaundice, vomiting promptly developed	6/14/37 6/24/37	4.2 3.0	8.2 6.2	144	..... +	Brown	0	1	Afebrile, few symptoms; suspected Laennec cirrhosis; complete recovery
19 ♀ 23 Negro	Secondary	June 1935, 3 weekly intravenous injections probably neoarsphenamine, 1 bismuth; no reactions; Sept. 1935, painless jaundice, light stools, itching, asthenia; no preceding cold	9/22/35 10/ 4/35 10/14/35	15.3 12.2 5.2	4.9 4.2	...	.....	Light brown	++++	2	Afebrile, slight anorexia; galactose test, 7 Gm. excreted; complete recovery
20 ♂ 37 Negro	Latent	Weekly intramuscular and intravenous therapy for one year beginning Oct. 1935; in Dec. 1936, 2 months after last injection, caught cold; abdominal distention, jaundice, light stools noted shortly thereafter	1/14/37 1/20/37 1/29/37	15.0 14.2 5.6	7.5 4.9 4.1	...	.....	Brown	++	1	Fever of 99 F., otherwise asymptomatic jaundice; complete recovery

to 6 per cent and reticulocytosis with values from 6 to 18 per cent during the first two weeks of hospitalization; reticulocyte counts to 4 per cent were also observed in case 5. Moderate to very marked increases in the erythrocyte sedimentation rate were noted in every case. Serologic tests for syphilis were positive in all instances except in case 7, although the infection appeared to be latent in many of the cases (table 1). The urine invariably contained bile pigment and in the earlier phases of illness in cases 1, 2, 5, 6 and 10 also contained faint to heavy traces of albumin. As indicated in table 1, the majority of patients showed little or no bile in the stools. Occult blood appeared in the stools in cases 1, 7 and 12. Gallbladder roentgenograms and duodenal drainage for evidences of stones uniformly gave negative results.

The acute constitutional and gastrointestinal symptoms initiating the reaction subsided after a few days or weeks, although in some instances low grade fever, anorexia or weakness continued. The later course of the reaction was characterized by painless jaundice of unusual duration (more than six months in cases 2, 4 and 7); and by relative freedom from associated symptoms except for the frequent occurrence of intense pruritus. The diminished bile content of the stools persisted and in many cases (table 1) was of such intercurrent colds, dietary indiscretions and the like that the chief role of arsphenamine may be to predispose the liver to "catarrhal" jaundice.

CHEMICAL CHARACTERISTICS OF POSTARSPHENAMINE JAUNDICE APPARENTLY DUE TO OBSTRUCTION OF THE INTRAHEPATIC BILIARY TRACT

As already indicated, we have employed the serum phosphatase determination (Flood and others,[3] Gutman and others[3]) and the cephalin flocculation test (Hanger[3]) to differentiate obstructive from hepatogenous jaundice. According to our experience (table 3), serum phosphatase levels greater than 10 Bodansky units signify that the icterus is probably of the obstructive type whereas values less than 10 Bodansky units point toward hepatitis. Applying this experience to the interpretation of our results in patients with postarsphenamine jaundice, we find that of the eleven cases in table 1 investigated, in ten there were serum phosphatase values greater than 10 Bodansky units per hundred cubic centimeters, i. e. levels consistent with obstructive jaundice. Of twenty-three other cases of postarsphenamine jaundice in which we have serum phosphatase determinations, cases not conforming to the syndrome of table 1, in eighteen serum phosphatase values were less than 10 Bodansky units, i. e. levels consistent with hepatogenous jaundice. The five exceptions include one case in which jaundice was shown at autopsy to be due to carcinoma of the head of the pancreas and not to the arsphenamine received; in another there was a late stage of pregnancy (case 17), and in the remainder there was an underlying Laënnec cirrhosis, all factors which independently may cause increased serum phosphatase activity.

TABLE 3.—*Results of Serum Phosphatase Determination and Cephalin Flocculation Test in Obstruction of the Extrahepatic Biliary Tract, in "Catarrhal" Jaundice and in Postarsphenamine Jaundice*

	Serum Phosphatase Activity *			Cephalin Flocculation Test					
	Number of Adult Cases Studied	Number with Values of 10.0 or More	Number with Values Less Than 10	Number of Adult Cases Studied	++++	+++	++	+	Negative or ±
1. Jaundice due to obstruction of the extrahepatic biliary tract (carcinoma head of pancreas, etc.)	79	72	7	77	0	0	1	6	70
2. "Catarrhal" jaundice (not due to known toxic agents)	69	7	62	60	37	11	6	2	4
3. Postarsphenamine jaundice (clinical history consistent with obstructive type)	11	10	1	8	1	0	0	0	7
4. Postarsphenamine jaundice (clinical history consistent with hepatogenous type)	23	5	18	7	2	3	0	1	1

* Serum phosphatase results expressed in Bodansky units per hundred cubic centimeters.

The cephalin flocculation test (table 3) has been carried out in seventy-seven cases of obstruction of the extrahepatic biliary tract, in seventy-six with negative or weakly positive reactions. Of sixty patients with "catarrhal" jaundice so tested, fifty-four gave definite flocculation whereas only six gave negative or 1 plus results, the latter chiefly patients first tested while jaundice was subsiding. Applying this experience to the interpretation of our results in postarsphenamine jaundice, we find that of the eight patients in table 1 subjected to this test, seven gave negative results, i. e. no evidence of liver parenchymal damage was obtained. On the other hand, of seven patients with postarsphenamine jaundice who did not fall in the group included in table 1, five gave 3 plus or 4 plus reactions, i. e. results consistent with jaundice of the hepatogenous type. The two exceptions were not tested until late in

By way of contrast with the clinical picture presented by the cases comprising table 1, we have summarized in table 2 the data of eight representative patients with postarsphenamine jaundice due to liver parenchymal degeneration ("hepatitis"). In the latter heterogeneous group of cases, jaundice may develop at any time during or after courses of treatment; there is no consistent relationship between the number of arsenical injections received and the appearance of symptoms. The reaction rarely begins so acutely, with shaking chills and fever. The clinical picture ordinarily is not that of obstructive jaundice, as in the cases in table 1, but is more consistent with hepatitis, often indistinguishable from that of "catarrhal" jaundice. In fact, as many investigators have emphasized,[4] icterus so frequently develops after

4. Herxheimer, Gotthold, and Gerlach, Werner: Ueber Leberatrophie und ihr Verhältnis zu Syphilis und Salvarsan, Beitr. z. path. Anat. u. z. Allg. Path. **68**: 93, 1921. Ruge, Heinrich: The Connection between Syphilis, Salvarsan and So-Called Catarrhal Jaundice on the Basis of 2,500 Cases Observed in the German Navy from 1919 to 1929, Urol. & Cutan. Rev. **36**: 355 (June) 1932. Wile, U. J., and Sams, W. M.: A Study of Jaundice in Syphilis: Its Relation to Therapy, Am. J. M. Sc. **187**: 297 (March) 1934.

the course of their illness when their jaundice was already subsiding and when the test is of little diagnostic value.

As is well known, the total cholesterol content of the blood serum tends to rise in patients with obstructive jaundice whereas normal or low values are observed in

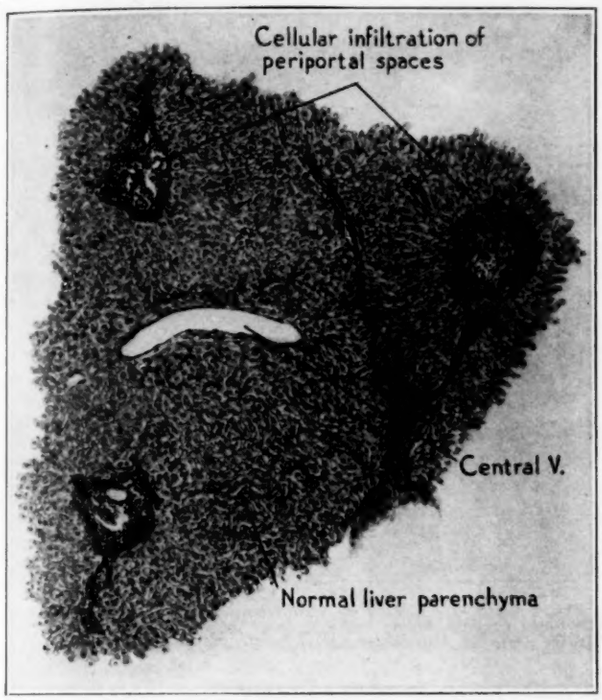

Fig. 1 (case 2).—Drawing of a low power field showing cellular infiltration of three periportal areas and normal liver parenchyma.

patients with jaundice due to hepatitis. Determinations of the total serum cholesterol were made for ten of the patients in table 1, of whom all but one (patient 2) showed levels of 250 mg. per hundred cubic centimeters or over while under observation, and in some instances extraordinarily high values were obtained. For reasons not apparent, the upward trend in serum cholesterol levels usually became more marked in the recovery phase of illness, when the serum bilirubin values began to fall. For patients with postarsphenamine jaundice not of the type included in table 1, normal or low cholesterol values were obtained (table 2), as in "catarrhal" jaundice.

A few "liver function" tests were performed and the results were consistent, on the whole, with the data already recorded. In cases 1, 3 and 12 values were 2.3, 2.2 and 5.3 Gm., respectively, with the hippuric acid test, as compared with 0.83 Gm. in case 13 of table 2.[5] Case 11 yielded a value of 0.87 Gm. with the galactose excretion test, as compared with 7.0 Gm. in case 19 of table 2. A slight rise in serum globulin to a level of from 3.0 to 3.5 Gm. per hundred cubic centimeters occurred in almost all cases in table 1, particularly in the late stages; this was associated with a moderate fall in serum albumin, so that the total serum protein values remained within normal limits. No significant increase in nonprotein nitrogen of the serum was noted. The arsenic content of the blood (in milligrams per hundred grams of dry blood) was determined in case 1 (trace), case 6 (0.1 mg.), case 10 (0.50 mg.) and case 11 (0.18 mg.), the normal range being from 0.01 to 0.08 mg.

5. Dr. Bruce Hogg furnished these values.

PATHOLOGIC FEATURES IN POSTARSPHENAMINE JAUNDICE APPARENTLY DUE TO OBSTRUCTION OF THE INTRAHEPATIC BILIARY TRACT

In cases 2, 7, 11 and 12 of table 1 operation and liver biopsies were performed. Dr. Alwin M. Pappenheimer and Dr. Virginia Kneeland Frantz gave the histologic descriptions, and Dr. Paul Klemperer reviewed the sections.

CASE 2.—At operation the liver was enlarged, not particularly firm and slightly darker than normal. The common duct was not obstructed or dilated and contained viscid bile. Several enlarged soft cystic lymph glands were seen. The gallbladder walls were somewhat pale and thickened and contained inspissated bile but no stones. Cholecystectomy was done, but subsequent microscopic examination revealed only mild chronic inflammatory changes.

Biopsy of the liver showed fair preservation of architecture. The liver cells appeared normal with vacuolations suggesting glycogen. There was slight but definite increase in fibrous tissue about the central veins and in the portal areas. A few proliferating bile ducts were seen. There was considerable inflammatory infiltration of the portal areas, chiefly lymphocytic with some polymorphonuclears (figs. 1 and 2). Polymorphonuclear cells were found within the walls and around the finer biliary radicles. The most striking feature of the section was the presence of patchy areas in which the bile canaliculi were markedly distended with bile plugs (fig. 3). Many Kupffer cells had taken up bile pigment. The diagnosis was pericholangitis and cholangiolitis.

CASE 7.—At operation Aug. 2, 1939, the liver was considerably enlarged. It seemed firmer than normal and was faintly bile stained, with a finely granular surface. The common duct was patent and of normal caliber. It contained a small amount of normal appearing bile.

Biopsy of the liver showed normal architecture. No necrosis of liver cells was seen. In some areas the liver cells and their nuclei were of larger than average size and stained more

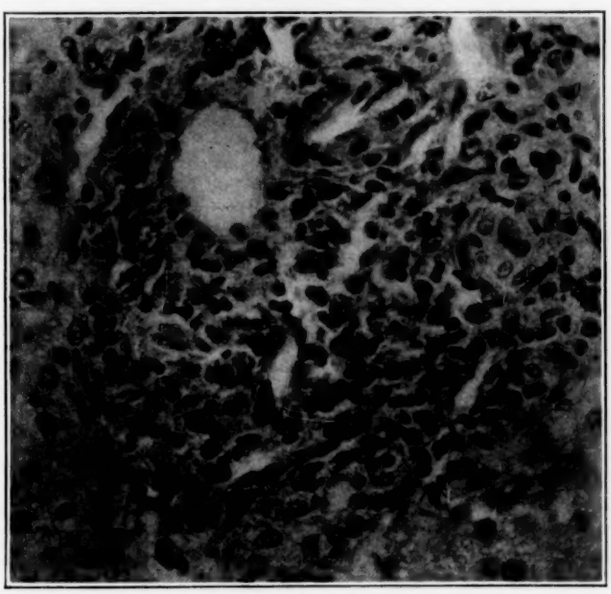

Fig. 2 (case 2).—Section of portal area showing infiltration with mononuclear and polymorphonuclear cells (high power).

intensely with eosin. The portal areas were extensively infiltrated by lymphoid cells and by moderate numbers of polymorphonuclears. There were many polymorphonuclear cells within the walls and around the finer biliary radicles. Perilobular connective tissue was not increased. There was marked stasis of bile as indicated by many large plugs in the canaliculi (fig. 4). Many of the Kupffer cells were loaded with bile pigment. The diagnosis was pericholangitis and cholangiolitis.

CASE 11.—At operation the liver was slightly enlarged, smooth and dark gray with a fine brownish mottling. The common duct was not obstructed or dilated. A large firm lymph gland was present at the junction of the cystic and common ducts. The gallbladder was adherent to the colon, was not distended and contained no stones.

Biopsy of the liver showed normal architecture. Except for sporadic cells showing homogeneous eosinophilic cytoplasm and nuclear degeneration, the liver cells appeared to be normal. There was no portal fibrosis. Bile plugs were present in many bile capillaries. In the portal areas there were scattered lymphocytes and occasional polymorphonuclears and eosinophils. There was some polymorphonuclear infiltration of the walls of the finer biliary radicles. Large mononuclear cells filled with bile were found near the central vines. The Kupffer cells also contained bile. The diagnosis was pericholangitis and cholangiolitis.

CASE 12.[6]—A specimen of liver for biopsy was obtained by aspiration [2] three weeks after the onset of jaundice.

The architecture of the liver was normal. There was no necrosis of the liver parenchyma. There was less cellular infiltration of the portal areas than in the preceding cases, but abnormal accumulations of round cells and polymorphonuclears and eosinophils were noted. The most striking feature was dilatation and engorgement of the finer biliary radicles with bile. A few of the liver cells and Kupffer cells contained bile pigment.

The essential features of the liver biopsy sections were (1) absence of significant parenchymal degeneration in intensely jaundiced patients; (2) cholangiolitis and pericholangitis of the nonsuppurative type (no infection of the biliary tree could be demonstrated), and (3) the presence of bile plugs in many of the bile capillaries, suggesting that the finer biliary radicles were the chief site of injury. Inflammatory changes about the bile passages and bile thrombi [7] within the lumen of the canaliculi apparently were the cause of obstructive jaundice.

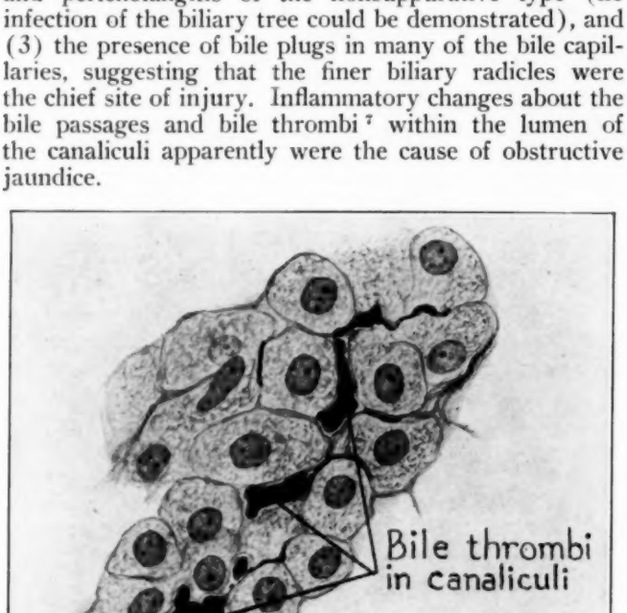

Fig. 3 (case 2).—Drawing of a high power field showing bile capillaries distended with bile thrombi.

These are not the usual features of arsphenamine hepatitis as reported in the literature or as observed at the Presbyterian Hospital. The histologic picture has been described, however, in association with nonarsphenamine jaundice,[8] as "cholangiolie" by Naunyn,[9] "primary intrahepatic cholangitis" by Siegmund [10] and by Eppinger as a "periacinar or cholangitic form of catarrhal jaundice." [11] Pericholangitis unassociated with disease of the extrahepatic biliary tract is probably not rare,[8] but marked lesions were found only twelve times

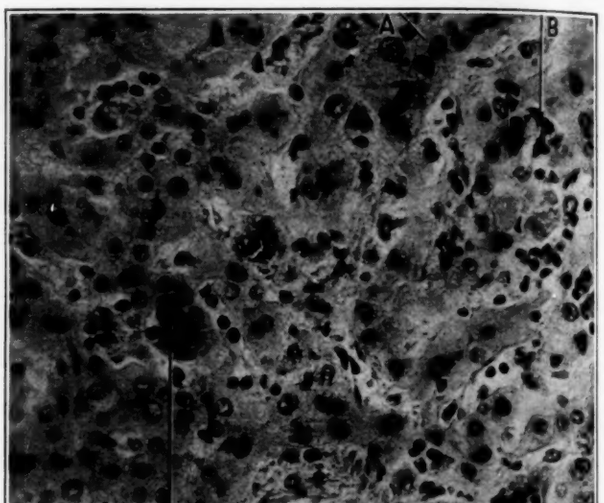

Fig. 4 (case 7).—Section of central portion of a liver lobule showing bile plugs in small biliary radicles. The Kupffer cells are mottled with bile pigment. *A*, bile in canaliculi; *B*, *B*, bile thrombi; *C*, central vein.

in 3,500 autopsies at the Presbyterian Hospital, occurring usually with terminal infections or cachectic states. No bile plugs were noted in the canaliculi in these cases.

COMMENT

In the cases described here an obstructive type of jaundice developed early in the course of treatment with arsenicals. Some of the cases reported in the literature as "early" or "intertherapeutic" postarsphenamine jaundice (Irgang,[12] Genner [13] and others) show the clinical features described in table 1, but we have been unable to find the obstructive type segregated as a distinct group. The cutaneous eruptions appearing in some of our patients were suggestive of "erythema of the ninth day," but jaundice is rarely associated with this condition.[14] The early febrile onset suggests the hepatic Jarisch-Herxheimer phenomenon; however, the usual explanation for this reaction—reactivation of syphilis or liberation of spirochetal endotoxins—can hardly account for the appearance of icterus in case 7, in which there was probably no syphilis.

We are unable to estimate the incidence of the obstructive form of arsphenamine reaction. The twelve cases comprising table 1 are from the records of ninety-two patients with postarsphenamine jaundice admitted to the Presbyterian Hospital from 1930 to 1939. Less

6. Dr. Theodore Rosenthal and Dr. William Curth of the Bureau of Social Hygiene, New York City, made this case available.

7. Hans Eppinger (Beiträge zur normalen und pathologischen Histologie der menschlichen Gallencapillaren mit besonderer Berücksichtigung der Pathogenese des Ikterus, Beitr. z. path. Anat. u. z. allg. Path. **31:** 230, 1902) and others have produced similar bile thrombi experimentally and believe that they are formed by the outpouring of coagulable protein into the injured ducts.

8. Klemperer, Paul: Pathology of Icterus, New York State J. Med. **33:** 1309 (Nov. 15) 1933.

9. Naunyn, Bernhard: Ueber Ikterus und seine Beziehungen zu den Cholangien, Mitt. a. d. Grenzgeb, d. Med. u. Chir. **31:** 537, 1919.

10. Siegmund, Herbert: Selbständige intrahepatische Cholangitis, Beitr. z. path. Anat. u. z. allg. Path. **87:** 425 (June 27) 1931.

11. Eppinger, Hans: Die Leberkrankheiten, Berlin, Julius Springer, 1937.

12. Irgang, Samuel: The Problem of Involvement of the Liver in Syphilis, Arch. Dermat. & Syph. **36:** 685 (Oct.) 1937.

13. Genner, Viggo: By-Effects in Salvarsan Therapy and Their Prevention wth Special Reference to the Liver Function, Copenhagen, Levin & Munksgaard, 1936.

14. Keim, H. L.: "Erythema of the Ninth Day" Following Administration of Arsphenamine, Arch. Dermat. & Syph. **31:** 291, 1935. Robinson, S. S.: "Erythema of the Ninth Day" Complicated by Acute Hepatitis and Jaundice on Continuation of Arsphenamine Therapy, ibid. **37:** 1031 (March) 1938.

severe forms of the reaction, with transient icterus not requiring hospitalization, doubtless occur. Mixed forms with concurrent parenchymal involvement, as indicated by a positive cephalin flocculation test, may also be encountered (case 10).

The nature of the toxic manifestations shown by the patients in table 1 is a matter of speculation. It seems unlikely from the evidence at hand that hepatic syphilis, arsphenamine overdosage and intercurrent "catarrhal" jaundice are important etiologic factors. The general pattern of the reaction has many of the characteristics of drug hypersensitiveness: 1. The initial injection of arsphenamine was without incident, but symptoms were precipitated by a second or third injection after a latent period. 2. The reaction was induced by relatively small amounts of arsenic. 3. In many cases there were associated cutaneous rashes, arthralgias, edema, eosinophilia and the like. 4. Further injections of arsenicals provoked more rapid and more severe recurrences of symptoms. It is known that after injection colloidal arsphenamine is rapidly stored in the Kupffer cells of the liver and other parts of the reticulo-endothelial system where degradation products are slowly formed. The original substance is relatively nontoxic to liver parenchyma, and the hepatic degeneration characterizing postarsphenamine hepatitis is usually attributed to diffusible derivatives.[13] Since parenchymal lesions are not striking in our cases it seems probable that the selective involvement of the finer biliary radicles represents a different type of toxic reaction induced in predisposed individuals by the freshly injected drug in colloidal form.[14a]

Selective injury of the finer biliary radicles, which is so striking in the liver biopsies of the arsphenamine cases described, may be produced by a number of toxic agents.[9] It has been observed in experimental toluylenediamine poisoning, a condition found by Bodansky[15] to be associated with unusually high serum phosphatase and cholesterol values. Dinitrophenol may also cause jaundice with clinical, chemical and pathologic features of intrahepatic biliary obstruction. We have recently observed such a case in which liver biopsy disclosed pericholangitis following the use of this drug as an antiobesic. Eppinger[11] has noted similar lesions in the liver in occasional cases of "catarrhal" jaundice of undetermined etiology and has pointed out the difficulties in distinguishing this group from cases of extrahepatic biliary obstruction.

TREATMENT

The recognition of the obstructive type of reaction is of some practical importance in the management of postarsphenamine jaundice. The administration of arsphenamine in these cases should be interrupted, perhaps discontinued. Although patients with some "early" types tolerate continuation of the drug, all of our patients reacted unfavorably when therapy was maintained.

The condition may be confused with obstruction of the extrahepatic biliary tract, and exploration may be performed for suspected common duct occlusion. No obstruction was found in our cases, but it is of interest that in case 2 noteworthy improvement followed cholecystectomy and liver biopsy. The therapy in these obstructive cases should be directed toward promoting drainage of the biliary tract rather than toward the conservation of injured liver parenchyma. Frequent large intravenous hypertonic dextrose infusions and choleretics, such as bile salt preparations, or cholic acid derivatives[16] should be given as early as possible after the appearance of jaundice.

SUMMARY

In twelve cases of postarsphenamine jaundice icterus was not of the usual hepatogenous type but appeared to be due to obstruction of the intrahepatic biliary tract. The clinical, chemical and pathologic features of this group suggest a distinct type of reaction to intravenous arsenicals characterized by:

1. Acute onset with constitutional and gastrointestinal symptoms coming on several hours after the second or third intravenous arsenical injection.
2. Appearance within several days of jaundice which may persist for weeks or months unaccompanied by other symptoms except pruritus.
3. Indications by various laboratory criteria of obstructive jaundice with little or no evidence of liver cell degeneration.
4. Preservation of essentially normal parenchyma in liver biopsies, the principal lesion being pericholangitis and bile thrombi in the finer biliary radicles.
5. Eventual recovery of the patient.

14a. Biedermann, A.; Hanssen, E., and Wright, H. N.: Relation Between Colloidal Properties and Toxicity of Arsphenamine and Neoarsphenamine, Proc. Soc. Exper. Biol. & Med. **31**: 172 (Nov.) 1933.

15. Bodansky, Aaron: Non-Osseous Origins of Serum Phosphatase: The Liver, Enzymologia **3**: 258, 1937.

16. Appel, Bernard, and Jankelson, I. R.: Treatment of Arsenical Hepatitis with Sodium Dehydrocholate: Experimental and Clinical Studies in Cases of Arsphenamine Poisoning, Arch. Dermat. & Syph. **32**: 422 (Sept.) 1935.

RANGE OF NORMAL BLOOD PRESSURE AND SUBSEQUENT DEVELOPMENT OF HYPERTENSION

A FOLLOW-UP STUDY OF 1,522 PATIENTS

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It is now well established that the systemic blood pressure is variable and that it reacts to various forms of external and internal stimulation. Such fluctuations of the blood pressure have contributed to the difficulty in determining normal blood pressure. Robinson and Brucer[1] have emphasized the difference of opinion as to what is normal blood pressure and have attempted in an extensive statistical study to determine more exactly the range of normal blood pressure. I have thought that if the range of variability of the blood pressure should be considered in addition to the level of blood pressure of any moment, some of the difficulties of determining whether or not an individual had normal blood pressure would be obviated. To use this conception, criteria for the normal range of blood pressure must be established. Some progress has been made regarding this through the use of standard tests for measuring the variability of the blood pressure (cold pressor test, breath-holding test) and by follow-up study of a group of subjects a number of years after the test was performed originally. The present study is an attempt to obtain further information about the normal range of blood pressure by determining the significance of elevation of the blood pressure in the upper ranges of normal as the result of the stimulus of a physical examination (nervous stress).

It has been the custom to regard transient elevations of blood pressure as of little significance. In fact some

From the Division of Medicine, the Mayo Clinic.

1. Robinson, S. C., and Brucer, Marshall: Range of Normal Blood Pressure: A Statistical and Clinical Study of 11,383 Persons, Arch. Int. Med. **64**: 409-444 (Sept.) 1939.

physicians seem to think that, if one or several readings of blood pressure within the accepted normal range are obtained, the possibility of a patient's having hypertensive disease is excluded. In various textbooks and articles on blood pressure are statements to the effect that the patient should be in a comfortable position and mentally at rest when the blood pressure is taken so that readings indicative of any transient elevation of the blood pressure may be avoided. My experience with the cold pressor test has led me to believe that

Table 1.—*Incidence of Subsequent Hypertension According to Original Systolic Blood Pressure*

Original Reading of Systolic Blood Pressure, Mm. of Mercury	10 Year Group			20 Year Group		
		Subsequent Hypertension			Subsequent Hypertension	
	Cases	Cases	Per Cent	Cases	Cases	Per Cent
Below 110	76	0	0	77	0	0
110-119	194	4	2.1	184	9	4.9
120-129	212	13	6.1	239	30	12.6
130-139	103	11	10.7	142	48	33.8
140-149	86	34	39.5	111	70	63.1
150-160	61	37	60.7	37	29	78.4
Total	732	99	13.5	790	186	23.5

any transient elevation of the systolic and diastolic blood pressure above a certain level should be regarded as evidence of a hyperreactive regulating mechanism for blood pressure and that in many instances this hyperreactivity is a precursor of sustained hypertension.

Previous studies concerning the significance of elevation of the blood pressure to the upper ranges of normal have consisted almost exclusively of analysis of insurance data in which the incidence of mortality has been used to determine the significance of different levels of high "normal" blood pressure. This method is open to obvious objection if an attempt is being made to determine the significance of an elevated blood pressure as to the probability of the development of subsequent hypertension. There has been no follow-up study of a large group of persons after a long period in which readings of blood pressure and examinations of the ocular fundi were used to indicate subsequent hypertension.

Diehl and Hesdorffer [2] have follow-up data on 155 students for seven years and they concluded that "young men who show persistent, intermittent or even transient elevations of blood pressure during their college years are much more likely to have elevated pressures after a period of from five to ten years than those in whom the blood pressure was consistently normal while they were in college." Palmer [3] studied the records of 3,598 routine physical examinations in the department of hygiene at Harvard University. He found a systolic blood pressure of more than 140 mm. of mercury in 10 per cent and of more than 150 mm. in 2 per cent. He obtained follow-up data after ten years on forty-nine of the persons with elevated blood pressure and sixty-six without elevated blood pressure and found that only 4.5 per cent of the latter had blood pressure of more than 140 mm., whereas 22.5 per cent of the group whose blood pressure was elevated originally had hypertension. He concluded that "if hypertension is found at 20 years of age it is somewhat more likely to be found persistent after ten years than it is to develop de novo during this interval."

2. Diehl, H. S., and Hesdorffer, M. B.: Changes in Blood Pressure of Young Men Over Seven Year Period, Arch. Int. Med. **52**: 948-953 (Dec.) 1933.

3. Palmer, R. S.: The Significance of Essential Hypertension in Young Male Adults, J. A. M. A. **94**: 694-697 (March 8) 1930.

As previously mentioned, Robinson and Brucer have made a detailed statistical study of the blood pressure of a large group of persons. They have concluded that the normal range of systolic blood pressure is between 90 and 120 mm. of mercury and that the normal range of diastolic blood pressure is between 60 and 80 mm. They probably have given a reliable estimation of the range of normal blood pressure under resting conditions, but their data will not indicate the possible significance of transient elevations of blood pressure of subjects whose blood pressure is usually normal, as they state "In all cases of abnormally high or low readings a reading was repeated as a check at the end of the examination to discount emotional or transitory rises, the lowest readings being recorded."

BASIS OF PRESENT STUDY

I noted that in many instances there was a correlation between the "ceiling," or maximal response, of the blood pressure of a patient to the cold pressor test and the first reading of the blood pressure taken on the same patient in the office at the clinic.[4] This correlation was noted also by Ayman and Goldshine [5] in their work with the cold pressor test. The first reading of blood pressure at the Mayo Clinic generally is taken by a physician with whom the patient is unacquainted and in strange surroundings. Consequently the first reading of the patient's blood pressure represents that individual's vasomotor reaction to nervous tension, which is in effect a psychic pressor test. This type of reaction is not as consistent as the response to a standard test like the cold pressor test, but it is sufficiently constant for the purposes of this study. Records of patients who have returned many years after their first examination at the Mayo Clinic are available in the files. By studying these records, it should be possible to determine whether or not hyperreactivity of the blood pressure to nervous stress is indicative of a prehypertensive phase

Table 2.—*Incidence of Subsequent Hypertension According to Original Diastolic Blood Pressure*

Original Readings of Diastolic Blood Pressure, Mm. of Mercury	10 Year Group			20 Year Group		
		Subsequent Hypertension			Subsequent Hypertension	
	Cases	Cases	Per Cent	Cases	Cases	Per Cent
Below 70	88	0	0	110	0	0
70 - 74	146	5	3.4	144	2	1.4
75 - 79	83	2	2.4	93	4	4.3
80 - 84	225	5	2.2	187	13	7.0
85 - 89	48	12	25.0	110	63	57.3
90 - 94	85	35	41.2	103	67	65.0
95 -100	57	40	70.2	43	37	86.0
Total	732	99	13.5	790	186	23.5

of essential hypertension. Furthermore, such data should give some indication of the prognostic significance of a borderline reading of blood pressure.

This study is based on review of the records in 1,522 cases. Two groups of cases were selected. In one group the patients had returned to the clinic ten years and in the other twenty years after their first examination. On their first visit to the clinic, which occurred either in 1916 or in 1926, the initial reading of blood pressure of all these patients was less than 160 mm. of mercury systolic and 100 mm. diastolic. The initial reading of the majority of patients was within the com-

4. Hines, E. A., Jr.: The Significance of Vascular Hyperreaction as Measured by the Cold Pressor Test, Am. Heart J. **19**: 408-416 (April) 1940.

5. Ayman, David, and Goldshine, A. D.: Cold as a Standard Stimulus of Blood Pressure: A Study of Normal and Hypertensive Subjects, New England J. Med. **219**: 650-655 (Oct. 27) 1938.

monly accepted normal limits, for only 4.4 per cent had blood pressure readings on the first visit of more than 145 mm. systolic and 90 mm. diastolic. None of them gave a history of previous hypertension or had pathologic conditions which might be said to have produced hypertension at the time or later, such as hyperthyroidism, toxemia of pregnancy or any renal or vascular disease.

The conclusions from this study are based on a comparison of the original reading of blood pressure as recorded on the first visit to the clinic and the presence or absence of hypertension when the patients were reexamined ten or twenty years later. The term "subsequent hypertension" as used in this paper implies one or several readings of blood pressure obtained at the time of the last visit in which the systolic blood pressure was more than 160 mm. and the diastolic more than 100 mm. In the majority of cases there was additional evidence of hypertension in the ocular fundi. This criterion is subject to some objection as it arbitrarily eliminated a few patients with a subsequent systolic reading of less than 160 mm. who definitely had hypertensive disease, as shown by evidence in the ocular fundi and by a diastolic reading of more than 100 mm. However, this group is so small that its inclusion among the group without subsequent hypertension has not materially affected the results.

TABLE 3.—*The Incidence of Subsequent Hypertension According to Original Blood Pressure*

Original Blood Pressure, Mm. of Mercury		10 Year Group			20 Year Group		
			Subsequent Hypertension			Subsequent Hypertension	
Systolic	Diastolic	Cases	Cases	Per Cent	Cases	Cases	Per Cent
Below 140	Below 85	514	12	2.3	506	19	3.8
Above 140	Below 85	28	0	0.0	28	0	0.0
Below 140	Above 85	71	17	23.9	136	68	50.0
Above 140	Above 85	119	71	59.7	120	99	82.5
Total.....		732	99	13.5	790	186	23.5

SUMMARY OF DATA

Of a total of 1,522 patients 614, or 40.3 per cent, were men and 908, or 59.7 per cent, were women. The average age of the women at the time of their first visit was 35.5 years and of the men 39.1 years.

The incidence of subsequent hypertension according to the original systolic and diastolic readings is given in tables 1 and 2. It will be noted that the higher the original reading of blood pressure the higher the incidence of subsequent hypertension. The small incidence of subsequent hypertension when the diastolic reading was less than 85 mm. at the time of the first admission is particularly striking. The incidence of subsequent hypertension when both the systolic and the diastolic readings at the first admission were considered is shown in table 3. When both the systolic and the diastolic readings were elevated, the incidence of subsequent hypertension was very great. Even when the systolic blood pressure was less than 140 mm., if the diastolic blood pressure was more than 85 mm. the incidence of subsequent hypertension was high. It is of particular interest that in the group of patients who had systolic blood pressure of more than 140 mm. but diastolic blood pressure of less than 85 mm. none had subsequent hypertension.

An analysis of the effect of age on the subsequent development of hypertension reveals that, if the blood pressure is elevated into the upper range of normal at the time of the original visit, the greater the age at that time, the greater will be the incidence of subsequent hypertension (table 4). However, in any given age group the general trend is for the development of subsequent hypertension among these patients who had a high normal blood pressure and for absence of subsequent hypertension among those who had low normal blood pressure. A more detailed statistical analysis of the effect of age on the blood pressure in this group is being carried out and will be reported at a later date.

Of the patients who were 50 years of age or more when the original reading of blood pressure was taken, seventy-three had hypertension ten or twenty years later. This does not support the idea that if a person is to have hypertension he necessarily should have it by the time he is 50 years of age.

The ocular fundi of 159 patients were examined at the time of the original visit. One hundred and thirty-one of the patients did not have hypertensive changes in the ocular fundi and in fourteen, or 11 per cent of these, hypertension developed subsequently. Twenty-eight had hypertensive changes, of grade 1 or 1+ in almost every instance, and in twenty-two, or approximately 80 per cent of these, hypertension developed subsequently.

That the group of patients with subsequent hypertension had a significant degree of hypertension is indicated by the fact that the mean blood pressure at the last examination for this group was 185 mm. systolic and 110 mm. diastolic. The systolic blood pressure of approximately 80 per cent was more than 170 mm. and of 38 per cent more than 190 mm. The diastolic reading of approximately 65 per cent was more than 110 mm. Approximately 70 per cent of the group with subsequent hypertension had examinations of the ocular fundi at the last examination; of these, 2 per cent had changes of group 4, 19 per cent changes of group 3, 43 per cent changes of group 2 and 36 per cent changes of group 1. The changes in the ocular fundi were those seen in Keith and Wagener's classification of hypertension groups 1 to 4.

TABLE 4.—*Incidence of Subsequent Hypertension Among Patients Who Had a High Normal Blood Pressure* *

Age, Years at Original Visit	10 Year Group			20 Year Group		
		Subsequent Hypertension			Subsequent Hypertension	
	Patients	Number	Per Cent	Patients	Number	Per Cent
10-19	0	0	0.0	2	2	100.0
20-29	5	3	60.0	19	11	57.9
30-39	22	9	40.9	35	29	82.9
40-49	51	34	66.7	42	35	83.3
50-59	32	17	53.1	19	19	100.0
60-69	8	7	87.8	3	3	100.0
70-79	1	1	100.0	0	0	0.0
Total	119	71	59.7	120	99	82.5

* Original blood pressure between 140/85 and 160/100.

SUMMARY

The records of 1,522 patients who returned to the clinic ten or twenty years after an original visit have been reviewed. An analysis has been made of the incidence of subsequent hypertension as correlated with the first reading of blood pressure recorded on the original visit. This first reading of blood pressure is thought to represent, in most instances, a response of blood pressure to nervous stress.

The results of this study support the idea that excessive variability or excessive responses of the usually

normal blood pressure to stimulation should be considered as evidence of a possible prehypertensive state. The range of normal blood pressure has not been definitely established by this study. However, patients whose blood pressures are not elevated, as a result of nervous stress, to more than 140 mm. of mercury systolic and (or) 85 mm. diastolic are unlikely to develop hypertension subsequently. If the blood pressure under such circumstances is less than 120 mm. systolic and 70 mm. diastolic, the patient is almost certain not to have hypertension subsequently. Conversely, even transient elevations of the systolic and diastolic blood pressures into the upper ranges of normal are prognostic of probable subsequent hypertension. Elevation of the systolic blood pressure alone is not indicative of subsequent hypertension. In this group of patients, 85 mm. marked a critical level of the diastolic pressure as to the possible occurrence of subsequent hypertension. It is recognized in this study that age is a factor in the incidence of subsequent hypertension; however, in general the results of this study hold true regardless of the age of the patient.

SELF-SELECTED DIETS IN TOXIC GOITER

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Normal limits of any physiologic factor are established from averages of measurements on normal subjects. For example, in determining the normal height of an individual at any given age the height values of normal persons of that age are averaged and tabulated. The same is true for determinations of normal weight or the normal metabolic rate and other measurements at various ages.

Following the same procedure it should be possible to establish the normal in diet by analyzing food mixtures representing self-selected diets consumed over, say, a three day period, using for this study persons of presumably normal health. By including in such studies individuals of different ages and occupations of normal life expectancy and reproductive capacities, it should be possible to determine if there is such a thing as a normal diet. In other words, do normal individuals living continuously in a state of good health instinctively select a diet containing proteins, fats and carbohydrates in percentages fairly constant in amount, or falling within narrow limits of percentage variations, to form what could be called a normal diet?

It would be difficult indeed to demonstrate that a diet established as normal by this method is injurious to a normal person. Certainly it is much easier to prove that various diseases and vague states of ill health develop among those who have been led or forced to adopt diets differing essentially from such an average, or normal, diet.

Where foods are available in normal variety and amount it appears that the instinctive control of food intake by the normal hunger sense is capable within wide limits of maintaining the individual in health for the average span of life. Nor does this instinctive control seem to be superior in animals or in savages whose dietary habits have been studied when compared with that of civilized man.

Despite changes caused by modern methods of food distribution and preparation, man still retains his ability to adapt himself to these changes. Instinct, however, is not an infallible guide and fails to ward off deficiency diseases, many of which become evident only after prolonged use of a diet lacking in certain necessary constituents.

How far, therefore, can one's hunger sense be trusted in the self selection of diet?

In testing the ability of rats and mice to choose between adequate and inadequate diets, Mitchell and Mendel [1] concluded that their results are in harmony with the conclusions earlier expressed by Osborne and Mendel that "the desire of a young animal for food is something more than the mere satisfaction of calorific needs. The demand made by the growth impluse must be met by a food of the proper chemical constitution."

Evvard [2] states that when the appetite is given full control of what shall be eaten it is surprising to note how pigs naturally select the food combination which swine herdsmen have long since approved of as the best and show a marked avoidance of those foods usually considered as ill adapted to swine.

Hutchinson [3] believes that the appetite of the growing child is far more reliable than the nutritional standards of either mother or physician.

Davis [4] reports experimental studies on self-selected feeding of newly weaned infants. Analyses of the foods were not made, but examination of their food records showed that in spite of the apparently chaotic manner of selection, their intakes of protein, carbohydrate and fat bore an orderly relation to each other and did not differ widely in the group.

On the basis of the average composition of 134,879 rations issued in 427 messes in different army camps, Murlin and Hildebrandt [5] report the average food consumption per man per day. In their investigation analysis of the food itself was made. They found that the food constituents averaged 14 calories of protein, 31 calories of fat and 55 calories of carbohydrates to every hundred calories of food ingested, i. e., on a percentage basis the food ingested was analyzed as 14 per cent protein calories, 31 per cent fat calories and 55 per cent carbohydrate calories.

Voit [6] gives the following ration for the use of a man at average hard labor: 16 per cent protein calories, 67 per cent carbohydrate calories and 17 per cent fat calories, the diet to contain 3,055 calories daily. For a man at hard work he allows 17 per cent protein calories, 58 per cent carbohydrate calories and 26 per cent fat calories in a diet containing 3,574 calories daily.

Lavonius [7] relates that champion wrestlers during their periods of effort ingest 18 per cent protein calories, 35 per cent carbohydrate calories and 47 per cent fat calories for a total of 5,070 calories daily. In another instance he found 18 per cent protein calories, 38 per cent carbohydrate calories and 44 per cent fat calories for a total of 4,254 calories daily.

Sundstrom [8] states that the diet of the average farmer of Finland contains 15 per cent protein calories, 64 per

1. Mitchell, H. S., and Mendel, L. B.: Am. J. Physiol. **58**: 211 (Dec.) 1921.
2. Evvard, J. M.: Proc. Iowa Acad. Sc. **22**: 400, 1915.
3. Hutchinson, Woods: We and Our Children, New York, Doubleday, Page & Co., 1911.
4. Davis, Clara M.: A Practical Application of Some Lessons of the Self-Selection of Diet Study to the Feeding of Children in Hospitals, Am. J. Dis. Child. **46**: 743 (Oct.) 1933; J. Am. Dent. A. **21**: 636 (April) 1934.
5. Murlin, J. R., and Hildebrandt, F. M.: Am. J. Physiol. **49**: 531 (Sept.) 1919.
6. von Voit, C., in Hermann, L.: Handbuch der Physiologie, Leipzig, F. C. W. Vogel, 1881, vol. 6, pt. 1, p. 519.
7. Lavonius, H.: Skandinav. Arch. f. Physiol. **17**: 196, 1905.
8. Sundstrom, S.: Untersuchungen über die Ernahrung der Landbevolkerung in Finnland, Helsingfors, 1908.

cent carbohydrate calories and 21 per cent fat calories in a total of 3,474 calories daily.

Pepe and Perelli [9] give a table showing the items composing the diets fed in a boys' colony which contained 16 per cent protein calories, 70 per cent carbohydrate calories and 10 per cent fat calories, and the diets fed in a girls' colony containing 15 per cent protein calories, 73 per cent carbohydrate calories and 8 per cent fat calories. These subjects were about 9 years old. The average daily number of calories for the boys was 2,212 and for the girls 1,827.

Mary Rose [10] gives a table to show distribution of calories as estimated by Professor Krogh, of the University of Copenhagen, for three types of diet, with high, medium, and low proportions of protein.

Here it is obvious that the protein content of the Eskimo diet is abnormally high simply because the diet of the Eskimo is not really self selected but is merely the only diet available to him. The same may be said of the low protein content of the diet of the Bengali. Indeed, the only apparent reason for the wide variations in percentage distribution seen in the diets of these and numerous other groups as presented in reports of similar kind is that the diets analyzed were imposed on the subject or were self selected only in a limited sense.

In reporting this study of the self-selected diets of persons of various ages and occupations attention is called to a noteworthy fact revealed by repeat or follow-up tests in any given case. These repeat tests have consistently shown that, within reasonably narrow limits of variation, the percentage of protein calories in the self-selected diet of a given subject is characteristic of the individual.

On the basis of caloric percentage (not grams per day), a given proportion of protein calories in the calories of the diet is habitually selected by one individual, while an entirely different percentage is quite as habitually preferred by another—provided, of course, that the subject is in physiologic balance.

The personal preference displayed by each is relatively constant and therefore dependable as a basis for classifying individuals in accordance with the data here

TABLE 1.—*Distribution of Calories in Typical Diets*

Type of Diet	Weight, Kg.	Protein, Gm.	Total Calories	Distribution of Calories, %		
				Protein	Fat	Carbohydrate
Eskimo.....	65	282	2,604	44	48	8
Bengali.....	50	52	2,390	9	10	81
European.....	70	118	3,055	16	17	67

reported. A very practical proof that it is constant is the fact that dietary habits may be redirected or changed only with difficulty and considerable perseverance, as those who have attempted to treat ailments due to dietary imbalances will agree.

One individual in this series, whose diet was analyzed in three day specimens on fourteen separate occasions at varying intervals over a four year period, showed a maximum of 13.2 and a minimum of 12.5 per cent protein calories, or an average variation of less than 0.4 per cent of the total calories. This record was achieved with no conscious attempt on the part of the subject to maintain regularity in the selection of food, either in kind or in amount.

9. Pepe, M., and Perelli, S.: Quaderni di nutrizione **4**: 327, 1937.
10. Rose, Mary S.: Foundations of Nutrition, ed. 3, New York, The Macmillan Company, 1938.

Analyses of food requirements of large groups of persons in health, as reported by other workers, very well show the average, or normal, percentage distribution of calories; but it is obvious that analyses of individual diets would be required to show if self-selected diets under some conditions tend to become unbalanced, and whether or not accurate measurements of such dietary imbalances have diagnostic value.

The purpose in presenting this paper, therefore, is to outline briefly the routine used in studying the dietary habits of individuals rather than groups, to determine whether or not any given deviation from the normal

TABLE 2.—*Method of Recording Experimental Data*

	Grams per Hour	Calories per Hour	Percentage of Total Calories
Urinary nitrogen.....	0.600	....	....
Dietary nitrogen.....	0.680	....	....
Protein.....	4.27	17.5	13.1
Fats.....	5.25	48.8	36.4
Carbohydrates.....	16.50	67.6	50.5
Salts.....	0.53	....	....
Total solids.....	26.55	133.9	....

diet is constantly associated with any group of symptoms, vague states of ill health or diseases of unknown origin.

One very practical application in connection with individual analyses of self-selected diets has already developed as a result of this method of approach. Preliminary data on that work are also included in this report.

COLLECTING THE FOOD AND URINE SPECIMENS

Each experiment was extended over a three day period. This tended to smooth out any irregularities in food intake and urinary nitrogen output, which often occur in shorter periods owing to variations in appetite or eating habits from day to day.

For obvious reasons it is necessary to employ only those subjects who, as determined by inquiry and checked by weighing at the beginning and end of the three day dietary experiment, show no recent consistent loss or gain in body weight.

Analysis of the self-selected diet begins with questioning the patient in detail and recording all answers regarding his eating habits. He is closely questioned concerning each meal of the day, as to what he eats, how much, or what size portions, how many times a week, how often he changes to a different type of meal, and what, how much and how often he takes of food or drinks between meals. This record of his own statement is filed for future use in checking against the food he brings in later.

The subject is then directed to maintain the same dietary habits and to refrain from any exercise, such as spring cleaning or gardening, not of his regular daily routine during the three day collection of the self-selected diet. He is provided with bottles to save all fluid foods separately—milk in one bottle, fruit juice in another, carbonated drinks in another, and so on. These have labels attached for recording separate daily amounts, to account for the three day total of each as they are accumulated for analysis. Fruit jars are used for saving moist foods, with labels attached for recording the meal and date. Dry foods are brought in wrapped, labeled and dated parcels.

Because the method of analysis requires drying to constant weight and because the protein content of alcoholic drinks is nil, these are not brought in but are

recorded and their caloric content is then estimated if they regularly make up any appreciable percentage of the diet. Coffee and tea drinks are not saved, but only the sugar and cream used in them.

Weighing the food to secure accurate duplicate portions interferes with spontaneous appetite and is therefore a handicap. With subjects of even moderate intelligence it is also unnecessary. The object in using the patient's food portions is not so much to duplicate the exact number of calories as it is to determine the percentage distribution of the calories. In other words, an error of a few grams in the weighing of any given serving of food affects the total of calories but does not appreciably affect the proportions of the protein, fat and carbohydrate calories in the final three day total of food.

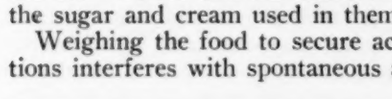

Fig. 1.—Electric food grinder (mounted through table top) for reducing food specimen to consistency of peanut butter.

As the subject serves himself he serves a similar portion into the food container, removing bones, gristle, fat, peelings or other inedible parts, exactly as he does from the portions he eats. If the subject fails to eat all of any serving, obviously a similar amount is removed from the portion to be put into the food container.

The food, when brought in these containers and kept separately, as directed, is in suitable condition to be inspected for the obvious purpose of determining whether it corresponds to the subject's own description of his diet. The food portions as they accumulate are kept under refrigeration to protect against fermentation.

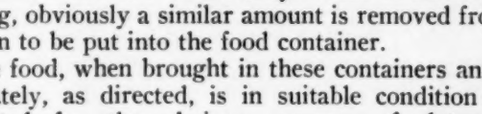

Fig. 2.—Electric stirrer and stirring vessel. For obtaining accurate duplicate checks, sampling must be done while food mass is kept in homogeneous state by rapid stirring.

The subject is also asked to save all metabolized nitrogen (urine) passed during this period, the total urinary nitrogen serving as a check on the food nitrogen, since approximately 90 per cent of the food nitrogen is absorbed, metabolized and then recovered in the urine. Thus, when the nitrogen recovered in the urine fails to equal approximately 90 per cent of the nitrogen found in the food specimen, the experimenter may know that (1) not all of the urine was saved, (2) servings of food were not duplicated, or (3) the subject either lost or gained weight during the three day period. It should be determined which of these possibilities actually occurred.

Rarely will patients deliberately deceive in saving the specimens of urine and food. They merely require instruction. When the routine and purpose are carefully explained to them repeat tests are not required more often than in any other form of quantitative studies.

The urine specimens are collected in gallon bottles and preserved against ammoniacal fermentation (loss of nitrogen) by the use of 15 Gm. of tartaric acid. A quart bottle collapsing into a close-fitting metallic or nonbreakable pitcher, the latter, in turn, closely fitting into a small case with a handle similar to the ordinary size compact, is provided for those obliged to be away from home during the three day period, as for work or for social engagements.

ANALYZING THE URINE

Many modifications of the regular Kjeldahl method (nesslerization and other methods) for determining total urinary nitrogen have proved unsatisfactory and should not be used. The allowable error here should not exceed 1 per cent. The original Kjeldahl routine giving this required accuracy may be found in any accepted laboratory manual.

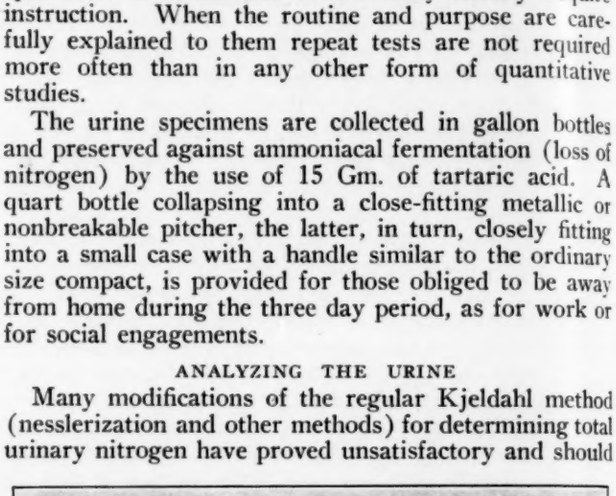

Fig. 3.—One hour's food portion: *A*, after grinding and drying to constant weight; *B*, after grinding by mortar and pestle, to obtain aliquot part for protein and fat determinations.

The nitrogen is computed on the basis that each cubic centimeter of tenth-normal acid neutralized by the ammonia distilled over is equal to 1.4 mg. of nitrogen in the 5 cc. of the mixed urine used in the analysis. Since the total seventy-two hour urinary volume is known, the number of milligrams of nitrogen per hour is easily calculated. The amount is then compared or checked against that found in the food specimen, to be analyzed as follows:

ANALYZING THE FOOD SPECIMEN

The entire seventy-two hour specimen of solid and liquid foods is put through a food grinder for reduction to peanut butter consistency. The mass as it comes from the grinder (fig. 1) is allowed to fall directly into a stirring vessel (fig. 2) of approximately 15 liter capacity and of known empty weight, which should be about 5 to 10 pounds (2 to 4 Kg.).

Ordinary tap water heated to 50 C. is used to wash into the stirring vessel all food adhering to the grinder. Then the same hot water is added until the mixture causes the vessel to weigh 10,080 Gm. more than its known empty weight. The reason for using hot water is

that it keeps the fats from separating out until duplicate specimens for analyzing have been secured.

The hot watery material is now stirred by an ordinary electric stirrer (fig. 2) until the entire mass is thoroughly mixed. Specimens for analysis are removed in duplicate and only while the mixture is being thoroughly stirred. Scales sensitive to within about 20 mg. at a 500 Gm. load are used for weighing the specimens to be analyzed. The total weight of the seventy-two hour mixture was purposely made 10,080 Gm. so that 1/72 of it, or a one hour food portion, would weigh 1/72 of 10,080 Gm., or 140 Gm. This 140 Gm. specimen is of convenient size for analysis and gives results directly in terms of units per hour, as in common use in metabolic studies. The 140 Gm. samples are weighed in flat bottom dishes of about 4 inch (10 cm.) diameter so as to facilitate evaporating the water later. To secure homogeneous and accurate duplicates, when dipping out these samples one uses a 300 cc. beaker, immersing it directly into the stirring mass.

As the mass is being poured into the flat bottom dishes for weighing the 140 Gm. samples, the watery mixture in the beaker is kept constantly stirred by spoon until the 140 Gm. tilts the scales. If more than 140 Gm. is inadvertently poured into the dish, the excess should not be removed without stirring the dish. When not so stirred with each removal to or from the sample during weighing, a portion taken from the top will be watery, or from the bottom will be more concentrated with solids, from rapid settling, and this will result in error due to sampling.

As an extra precaution, about 1 liter of the stirred seventy-two hour specimen is removed to a wide mouth, screw cap jar and kept in reserve in the ice box for emergency, against a need for repeat analysis.

The duplicate 140 Gm. samples are kept in a drying oven at 70 C. for forty-eight hours. The solids, ranging from 10 to 35 Gm., should check within less than 1 per cent in the duplicates. After removal from the dish and grinding by mortar and pestle a granular product is obtained; this is remarkable in its similarity to other specimens in all types of cases and in its close resemblance to grapenuts in consistency, color, odor and taste (fig. 3).

An aliquot part, a convenient, 10 Gm. quantity, is used for extracting the fat with ether by the Soxhlet apparatus. Similarly, an accurately weighed 1 Gm. portion of the sample is used for total nitrogen determination by the method used for analyzing the urine, except that 4 drops of a saturated solution of copper sulfate is added to hasten the oxidation by sulfuric acid and the additional food materials are subjected to continuous heating for from one and one-half to two hours, or until the blackened mixture becomes only slightly straw colored.

By calculation the grams per hour of fat (Soxhlet extraction) and grams per hour of protein (Kjeldahl) in the one hour's portion of food may thus be determined. The weight of the total solids minus the combined fat and protein weights gives the weight of the carbohydrates and salt. (Fibrous vegetables and other residue, when thus dried to constant weight, form an unimportant fraction of the total solids of the sample).[11] Salt content is approximated as 2 per cent of the total dried mass, so that the latter, minus the weight of the proteins, fats and salts, gives the weight of the carbohydrates. Table 2 illustrates the method of recording the essential data and computation of the percentage distribution of protein, fat and carbohydrate calories.

The figures in table 3 showing the percentage distribution of calories in normal subjects are in good agreement with the averages of those who have reported analyses of the diets of groups of normal, active persons. The averages for the group, 14.4 per cent protein, 34.7 per cent fats and 50.6 per cent carbohydrates, do not vary appreciably from the group averages reported by Murlin and Hildebrandt to which reference was made in a preceding paragraph. Individual variations from these averages are also without significance.

TABLE 3.—*Distribution of Calories in the Diet of Normal Subjects*

Case	Subject	Occupation	Sex	Age	Percentage of Calories		
					Protein	Fat	Carbohydrate
1	C. A.	Carpenter	♂	28	15.0	38.2	46.8
2	B. A.	Bookkeeper	♀	30	14.9	37.7	47.4
3	M. A.	Housekeeper	♀	62	15.1	36.1	48.8
4	P. A.	Storekeeper	♂	37	15.0	35.0	50.0
5	J. J. B.	Chemist	♂	26	16.7	37.6	45.6
6	Bares	Salesman	♂	44	14.8	38.6	46.6
7	J. B.	Foundryman	♂	56	14.6	44.8	40.6
8	M. B.	Lawyer	♂	45	16.1	35.0	48.9
9	S. C.	Physician	♂	40	13.3	36.0	50.7
10	W. C.	Attorney	♂	61	13.0	37.2	49.8
11	M. C.	Typist	♀	20	14.9	37.5	47.6
12	D. C.	Mechanic	♂	20	14.0	39.6	45.4
13	W. C.	Gas station attend.	♂	23	15.5	35.8	48.7
14	J. C.	Salesman	♂	30	14.7	40.1	45.2
15	M. C.	Nurse	♀	30	14.3	36.2	49.5
16	A. D.	Mechanic	♂	16	15.0	29.6	55.4
17	H. D.	Typist	♀	23	15.4	31.0	53.6
18	R. D.	Mechanic	♂	16	14.3	32.7	53.0
19	T. D.	Mechanic	♂	16	13.4	35.2	51.4
20	E. D.	Machinist	♂	26	14.8	32.2	53.0
21	Dick	Machinist	♂	20	13.6	35.1	51.3
22	M. E.	Housemaid	♀	35	13.8	39.2	47.0
23	E.-1	Physician	♂	26	13.5	35.9	50.6
24	E.-2	Housekeeper	♀	36	13.7	37.2	49.1
25	E.-3	Housekeeper	♀	26	14.3	31.1	54.6
26	E.-4	Salesman	♂	27	13.1	32.0	56.9
27	E.-5	Physician	♂	35	13.3	38.2	48.5
28	C. F.	Mechanic	♂	19	14.2	37.2	48.6
29	R. F.	Stenographer	♀	25	12.5	34.6	52.9
30	M. G.	Housekeeper	♀	30	15.8	36.9	47.3
31	B. G.	Housekeeper	♀	30	14.0	30.2	55.8
32	R. G.	Schoolboy	♂	17	14.0	39.1	46.9
33	A. D. H.	Chemist	♂	22	15.5	35.8	48.7
34	A. H.	Shipping clerk	♂	18	12.6	29.2	58.2
35	D. S. J.	Physician	♂	30	12.8	40.1	47.1
36	B. J. J.	Schoolgirl	♀	8	15.9	41.0	44.1
37	H. M. J.	Physician	♂	52	17.1	37.3	45.6
38	B. J.	Schoolboy	♂	14	15.6	37.8	46.6
39	J. K.	Housekeeper	♀	..	12.8	34.6	53.3
40	I. N.	Mechanic	♂	22	14.5	38.2	47.3
41	A. R. N.	Salesman	♂	37	12.8	35.3	52.0
42	N.-A.	Housekeeper	♀	..	14.9	39.2	45.9
43	B. P.	Salesman	♂	32	15.5	36.0	48.5
44	T. P.	Housekeeper	♀	50	14.4	36.0	49.6
45	S. R.	Secretary	♀	..	13.0	39.2	47.8
46	L. S.	Technician	♀	20	14.9	35.1	50.0
47	P. S.	Storekeeper	♂	28	12.8	28.1	59.1
48	W. S.	Errand boy	♂	22	12.3	35.8	51.9
49	R. W.	Mechanic	♂	23	12.8	35.9	51.3
50	E. W.	Machinist	♂	23	15.5	32.3	48.5
		Average			14.4	34.7	50.6

The beginning of this study was the observation that toxic goiter patients show a smaller urinary nitrogen output in proportion to their larger caloric intake than do normal subjects.

Naturally the suspicion arises at once that this smaller urinary nitrogen output per caloric intake is due to a protein deficiency in the diet of the toxic goiter patient. To demonstrate this protein deficiency in the diet it was necessary to make routine food analyses of the self-selected diets of toxic goiter patients showing varying degrees of thyroid enlargements, different types of goiters and all possible grades of toxicity.

For this study it was necessary to eliminate all goiter patients except those in whom all signs and symptoms necessary for an easy diagnosis of hyperthyroidism were present.

11. Atwater, W. O., and Woods, C. D.: The Chemical Composition of American Food Materials, Bulletin 28, United States Department of Agriculture, Office of Experiment Stations, 1896, p. 13.

Table 4 gives sufficient data to express the relative degree of toxicity together with the data obtained from analysis of the self-selected diet in each individual case. Comparing the normal series in table 3 with the toxic goiter series in table 4, it will be observed that no normal subject consumed as little as 12 per cent, whereas no goiter subject consumed as much as 12 per cent, of his calories as protein. In other words, owing to his high metabolism, the toxic goiter patient may consume more nitrogen per day, but the diagnostic point is that he consumes less nitrogen per calory than does the normal subject.

It may be argued that this preference for a diet low in protein is due to a craving for concentrated foods to maintain the increased metabolism. The difficulty with that explanation, however, is that even after thyroidectomy and after the usual drop to a subnormal basal metabolic rate, i. e. when all need for food concentrated in calories is past, a high percentage of patients will persist in this preference for a low protein diet for months or perhaps for the remainder of their lives.

Moreover, the total calory requirement of the toxic goiter patient is frequently even smaller than that of a normal subject of equal size, thus showing that high calory demand does not explain this peculiar imbalance of the protein portion of the diet.

TABLE 4.—*Distribution of Calories in the Diets of Hyperthyroid Patients*

Case	Subject	Sex	Age	Basal Metabolic Rate, Plus	Signs and Symptoms				Percentage of Calories		
					Pulse	Thyroid Enlargement	Tremor	Type of Goiter	Protein	Fat	Carbohydrate
1	Armstrong	♀	50	49	120	Large	+++	Mixed	8.1	32.8	59.1
2	Baker	♀	41	37	88	Large	++	Toxic adenoma	6.8	38.0	55.2
3	E. B.	♀	35	22	85	Visible	+	Toxic adenoma	9.7	35.0	55.3
4	F. C. B.	♀	43	27	104	Visible	++	Exophthalmic	9.6	38.2	52.8
5	Blank	♀	50	14	94	Visible	+	Exophthalmic	11.1	32.1	56.8
6	Bryan	♀	37	50	98	Medium	++	Mixed	10.1	40.1	49.8
7	Capone	♀	54	66	124	Very large	++	Toxic adenoma	7.1	35.3	57.6
8	Eggleston	♀	45	18	92	Very large	+	Toxic adenoma	9.2	38.8	52.0
9	W. E.*	♂	53	28	86	Unilateral	+++	Exophthalmic	10.0	35.2	54.8
10	Fr. F.	♂	34	14	88	Large	++	Toxic adenoma	10.4	33.6	56.0
11	Fobes	♀	45	22	96	Large	+	Toxic adenoma	9.1	36.2	54.7
12	M. Frank	♂	42	29	106	Large	++	Toxic adenoma	10.1	35.3	54.6
13	M. Fried	♀	24	63	124	Unilateral	+++	Exophthalmic	9.3	45.0	45.7
14	Goldstein	♂	50	65	84	Large	++	Toxic adenoma	10.6	38.7	50.7
15	Hojnar	♀	45	29	80	Visible	?	?	7.9	31.4	60.7
16	Holmberg	♂	46	28	104	Visible	++	Toxic adenoma	10.7	36.6	52.7
17	E. H.	♀	40	34	92	?	?	?	7.5	32.1	60.4
18	H. I.	♀	20	62	106	Large	+++	Exophthalmic	9.0	26.4	64.6
19	Jaroski	♀	29	12	88	Palpable	+	?	8.9	35.0	56.1
20	Klein	♀	25	85	140	Very large	+++	Exophthalmic	10.3	33.5	56.2
21	M. L.	♀	38	13	93	Visible	++	Toxic adenoma	9.3	24.6	66.1
22	F. L.	♀	30	14	102	Large	+	Toxic adenoma	8.3	39.7	52.0
23	Lawall	♂	24	31	90	?	?	?	10.1	36.2	53.7
24	K. L.	♀	30	16	80	Medium	+	?	9.2	34.1	56.7
25	W. A. L.*	♀	43	90	112	Large	+++	Exophthalmic	9.9	43.6	46.5
26	F. L.	♀	39	35	120	Medium	+++	Mixed	11.0	45.2	43.8
27	C. mM.	♂	34	46	122	Large	++	Toxic adenoma	10.0	30.7	59.3
28	McC.	♀	67	43	108	Large	+++	Mixed	10.3	42.4	47.3
29	S. N.	♂	56	53	92	Medium	+++	Mixed	9.3	33.2	57.5
30	G. N.	♂	24	35	96	Medium	++	Mixed	10.5	20.0	69.5
31	S. P.	♀	59	33	96	Medium	++	Exophthalmic	10.1	38.2	51.7
32	Paulick	♀	52	39	110	Medium	++	Toxic adenoma	10.1	27.1	62.8
33	Risberg	♀	56	18	108	Egg size	+++	Toxic adenoma	10.3	35.2	54.5
34	Rooks	♀	47	34	88	?	?	?	6.3	30.7	63.0
35	Slaughter	♀	41	23	102	Large	+++	Toxic adenoma	8.0	29.2	62.8
36	F. T.	♀	33	36	104	Large	++	Exophthalmic	10.0	32.0	58.0
37	Todd *	♀	40	55	104	Medium	+++	Exophthalmic	8.3	36.4	55.3
38	Ward	♀	26	25	100	Visible	?	?	10.0	40.3	49.7
39	Whitney	♂	58	32	96	Large	+++	Toxic adenoma	9.2	38.7	52.1
40	Stricker *	♀	33	12	96	Medium	?	?	9.6	30.6	59.8

* Recurrent goiter.

CLINICAL APPLICATION

Thyroid enlargement as a sign of toxic goiter is too variable to be of much value in diagnosing hyperthyroidism of any degree, especially if the disease is just beginning. Many workers also admit the possibility of the presence of toxic goiter in beginning or subclinical form in individuals showing normal basal metabolic rates. Thus, if the basal metabolic rate before the onset of goiter is, say, —15 per cent in a given case, a beginning toxic goiter could cause the rate to increase several points and yet be found within normal limits at the time of examination, despite the beginning hyperthyroidism.

The clinical application of this relationship between protein dietary imbalance and toxic goiter is, therefore, its diagnostic use in cases characterized by marked fatigue, emotional instability and other symptoms of toxic goiter, but in which thyroid enlargement is doubtful and the basal metabolic rate is "normal." In every medical practice there is a high percentage of these cases showing all variations of this symptom complex. They have been variously diagnosed as hypochondria, autonomic imbalance, neurasthenia, effort syndrome and fatigue neurosis.

From this study it appears that they may be classified under one heading, namely, subclinical goiter. Besides resembling the clinical stage of toxic goiter except in thyroid enlargement and increased basal metabolic rate, this condition shows an additional point of similarity to toxic goiter, namely, an identically similar habitual protein deficiency (below 12 per cent protein calories) in the self-selected diets of such patients.

These physically depressed, emotionally unstable patients in any medical practice greatly outnumber the clinically toxic ones, just as do those with subclinical rickets, subclinical pellagra or any nutritional disease in which the beginning manifestations evolve progressively to an entirely different final picture in its full-grown stage.

The number of such cases encountered in this study have outnumbered the forty cases of clinically toxic goiter listed in table 4 by about five to one. The record of this larger series and a description of the surprisingly good therapeutic results achieved through the use of a

normal protein diet in these cases (including cases of persistent and recurrent toxic goiter following thyroidectomy) cannot logically be included in this report. They will be presented in a future paper, together with the description of a greatly simplified laboratory routine for measuring protein deficiency in both clinical and subclinical toxic goiter without the use of the complicated procedures required for collection and analysis of all of the diet in the work here reported.

CONCLUSIONS

The results of 233 analyses of the self-selected diets of 154 normal, healthy subjects of various ages, races and occupations, and 117 analyses of the diets of forty toxic goiter patients have shown that each individual is guided by personal food preference to select a diet which he maintains at a relatively constant protein percentage and at a level characteristic of himself.

A protein content of 13 per cent is sufficient; one of 11 per cent is insufficient, and yet the individual who prefers the 11 per cent diet, when placed on a diet containing 13 per cent will unconsciously tend to revert to the 11 per cent level without the remotest idea as to how much protein either diet contains.

Once this subconsciously operating personal food preference becomes inaccurate in its selection of a proper protein percentage, it may be reeducated or redirected to its former degree of accuracy only with considerable coaching and perseverance. Indeed, the subconscious reactions which determine the level at which this constant protein percentage shall be established by the individual apparently lie deeper than mere temporary physiologic need, indicating that neither personal food preference, hunger nor appetite are to be trusted implicitly in the self selection of diets.

SUMMARY

Analysis by others of the total food consumed by large groups of active, normal persons has established the normal protein content at from 13 to 17 protein calories per hundred calories of food, i. e., from 13 to 17 per cent protein calories.

A routine was adopted for collecting and analyzing the self-selected diet in determining how far the individual has deviated from this normal in his dietary habits.

It is noteworthy that the lowest reported normal protein value is 13 per cent. A habitual personal preference for a diet containing appreciably less than this minimal limit of 13 per cent protein calories is of clinical importance because of its ultimate effect on health.

Persons suffering from toxic goiter—regardless of age, sex or type of goiter—uniformly show a tendency to select a diet below this minimal limit of 13 per cent protein calories.

When put on a diet containing the normal percentage (13 per cent) of protein the toxic goiter patient tends constantly to revert to his own preference for the subnormal protein diet.

Preference for a low protein diet persists in variable degree even after subtotal thyroidectomy in a high percentage of cases and is uniformly associated with unfavorable postoperative results, such as fatigue and susceptibility to cold, and in some cases with actual recurrences of the disease.

315 South Honore Street.

CONTRACEPTION: A STUDY OF FIVE HUNDRED CASES FROM PRIVATE PRACTICE

CLINICAL OBSERVATIONS

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NEW YORK

An analysis of 500 private contraceptive cases selected at random from my files is presented. This study shows the extent and types of contraception practiced during a twelve year period, before and after medical consultation, by a group of middle class New York city families of different religious denominations, all of whom were white but three.

I interviewed each of the 500 women in this study and gave a general physical examination, including a bimanual pelvic examination.

TABLE 1.—*Reasons Patients Requested Contraceptive Advice*

1. Recent childbirth		
2. Desire to space offspring		
3. Desired number of children already born		
4. Medical condition of wife, e. g., hyperthyroidism, nephritis, tuberculosis, diabetes, heart disease, deaf-mutism, blindness or convalescence after acute illness such as typhoid fever or pneumonia, or after surgical procedure such as appendectomy, or rectal fistula		
Medical condition of husband, e. g., heart disease, tuberculosis, convalescence from surgical procedure or acute illness		
5. Mental illness or emotional disturbance of husband or wife		
6. Economic conditions	(*a*) Unemployment of husband	
	(*b*) Wife sole or co-wage earner	
	(*c*) Support of dependents	
	(*d*) Desire to complete education or professional training	
	(*e*) Indebtedness	
7. Dissatisfaction of either or both partners with method of contraception employed		
8. Failure of method employed		

TABLE 2.—*Marital Status at Time of Consultation for Contraceptive Advice*

Marital Status	Number of Women		Per Cent
Married	368		73.6
Unmarried	132		26.4
(*a*) Engaged	93	19.2	
(*b*) Unattached	39	7.2	
Total	500		

The purpose of this clinical study was to ascertain the extent and efficiency of contraceptive efforts and their influence on fertility and marital happiness. The results of medically prescribed contraceptive methods are compared with self-prescribed methods. The health problems involved are summarized.

A variety of factors which might affect the health of the wife, the size of the family and marital happiness were studied. Information was obtained about the physical and emotional health of the husbands and wives, their social, economic and educational status and their religious beliefs. Intimate facts are given regarding their sex habits, contraceptive methods, failure and success of contraceptive methods, size of families, number of planned and unplanned pregnancies, number of abortions, premarital sex experiences, frequency of coitus, frequency of orgasm, sexual compatability, pelvic pathologic conditions and other factors, and conclusions are summarized in the accompanying tables.

Read before the International Congress of Biophysics, Biocosmics and Biocracy, New York, Sept. 13, 1939.

The majority of women in this study (368) consulted a physician for contraceptive advice after marriage. The largest number (125) applied during the first year of marriage, the second largest group (ninety-four) came between the second and the fifth year and a close tie were ninety-three women who came premaritally. By

TABLE 3.—*Duration of Marriage at Time of Consultation*

Number of Years Married	Number of Women	Cumulative Totals of Number of Women
1 day to 1 month	46	...
1 to 6 months	51	...
7 to 12 months	28	...
During 1st year	125	...
Total married 1 year	...	257
1 to 5 years	94	...
Total married 5 years	...	351
6 to 10 years	68	...
Total married 10 years	...	419
11 to 15 years	42	...
Total married 15 years	...	461
16 to 20 years	21	...
Total married 20 years	...	482
21 to 30 years	5	...
Total married 30 years	...	487
Unknown	13	...
Total	...	500

TABLE 4.—*Religious Distribution*

Denomination	Number of Men	Number of Women
Hebrews	259	245
Protestants	156	175
Catholics	59	58
Unstated	26	22
Mixed marriages: Hebrew and Catholic	5	
Hebrew and Protestant	1	

the end of the fifth year 351 had applied and after ten years 461 had asked for medical aid in controlling reproduction. In recent years there has been an increased trend toward seeking contraceptive advice prematurally. The ideal time to give medical contraceptive advice is prematurally if conception must be avoided for health reasons. Sixty-eight women applied ten years and twenty-six came between sixteen and thirty years after marriage. Thirty-nine single (unattached) women requested contraceptive advice.

The majority of women (91 per cent) were married before 35 years of age; of these 44 per cent married before 25, 16 per cent married between 35 and 50, 8 per cent married between 36 and 40 and 7 per cent between 40 and 50. Two-tenths per cent married after 50.

Eleven wives were from one to six years older than their husbands, all others the same age or younger. In one case only was there a great difference — that of a man of 50 with a wife of 25 years.

The husbands ages ranged from 17 to 60 years. The majority of men, 207, or 40.5 per cent, married before 29 and 176, or 38.1 per cent, between 30 and 40 years; while a minority, sixty-six, or 14.3 per cent, married between 40 and 60. Most men who intended to marry did so before 40 years. The majority of women in this study married earlier, before 25, while the majority of men married between 25 and 35. By the age of 35 the majority of men and women were married.

Over half the women in this series were gainfully employed of necessity and were co-wage earners. (These figures may be higher because of the larger number of young wives.) Ninety per cent of the premarital group stated that they would have to continue working after marriage and 10 per cent wished to do so. Economic insecurity was the biggest single factor given for seeking contraceptive advice and avoiding immediate pregnancy. Every premarital couple expressed the request that the method prescribed should not cause sterility and stated that they hoped to be able to plan a pregnancy as soon as their financial status would allow them to rear a child according to desirable standards of living.

Of the 229 who admitted adequate income, many stated that they already had all the children they could afford or that they wished to space further pregnancies scientifically for health or social reasons.

Thirty-eight per cent of ninety-three engaged couples who came for a premarital medical consultation admitted premarital sex relations, mostly during the engagement period, whereas 62 per cent denied premarital sex experience. Of those married at the time of consultation only 9.2 per cent admitted premarital sex relations whereas 91 per cent denied them. Seventy-seven women, or 15 per cent of the 500 women, were virgins. Of these there were 6.5 per cent married virgins and 57 per cent of the engaged with intact hymens.

(Since the study of 500 cases, another study of 170 premarital couples seen from January 1938 to December 1939 was made. Premarital sex relations were admitted by 36 per cent of the females and 51 per cent of the males. Of this group 100 were college graduates, sixty high school graduates and 9 elementary school graduates between 18 and 35 years of age. Forty-one virgins of this group required medical dilation of the hymen due to various anatomic reasons, such as small hymenal opening, and eighty-eight after medical inspection were told they required no medical stretching of the hymen and introitus.)

TABLE 5.—*Age of 461 Couples at Marriage*

Age	Number of Men	Percentage of Men	Number of Women	Percentage of Women
15-19	1	0.2	1	0.2
20-25	82	17.7	205	44.4
26-30	125	27.1	108	23.4
31-35	120	26.0	107	23.2
36-40	56	12.1	39	8.4
41-50	61	13.2	34	7.3
51-60	5	1.08	1	0.2

TABLE 6.—*Employment of Wives in Relation to Duration of Marriage*

Total number of women employed	276
Married women employed	144
Premarital group of women planning to continue employment after marriage	132

TABLE 7.—*Relation of Combined Incomes to Number of Children Desired (Planned Future Pregnancies)*

Total number of women	500
Combined incomes held inadequate	244
Combined incomes held adequate	229
Unknown	27

Either a much larger percentage of engaged couples are having premarital sex relations today as compared with the past, or the older married women are less frank in discussing this phase of their sex life.

Twenty-four married women required dilation of the hymen or removal of a septate band by electric cautery, at periods after marriage varying from one day to sixteen years. This was accomplished as an office

procedure usually in one medical visit. All needed psychotherapy to overcome fear of pain with coitus and instruction regarding male and female genital anatomy and sex technic. Only one patient required hospitalization and surgical dilation under nitrous oxide-oxygen anesthesia.

TABLE 8.—*Premarital Sex Relations and Virginity*

Status	Number Admitting Relations	Per Cent	Number Denying Relations	Per Cent	Intact Hymens	Per Cent
93 engaged women....	40	38.0	59	62.0	53	57.0
368 married women....	33	9.2	335	91.0	24	6.5

TABLE 9.—*Nonconsummation of Marital Relations in Married Women*

(Duration of Marriages and Causes)

Number of Married Virgins	Duration of Marriage at Time of Consultation
4	1 week
2	2 weeks
2	3 weeks
2	1 month
3	2 months
1	3 months
2	6 months
1	11 months
3	1 year
1	3 years
1	7 years
1	10 years
1	16 years
Total 24	

Causes of Nonconsummation
1. Septate hymen
2. Tight thick hymen
3. Fear of pain or inability to stand pain
4. Ignorance of sex technic, either partner
5. Ignorance of genital anatomy
6. Fear of pregnancy
7. Sense of shame regarding genitals and coitus

The frequency of coitus in married couples before medical consultation was most often (39 per cent) twice a week, next (23 per cent) three times weekly and (19 per cent) once a week. Six per cent had daily sex relations while 2.3 per cent abstained. The majority of couples, 130, or 78 per cent, had intercourse more than once a week.

The use of prescribed contraceptive methods did not vary the frequency of coitus when sex habits had been established. The only significant change was the fact that only 0.5 per cent continued abstinent after the consultation whereas 2.3 per cent had had no sex relations before.

Twenty-six (10.3 per cent) single women had been pregnant once out of wedlock, nine women during their engagement period and fourteen unattached women. Two unmarried women had been pregnant twice. One single woman had been pregnant four times.

Of 500 women of childbearing age in this study, 368 were married at the time of consultation and 132 were unmarried. Ninety-three engaged women came for premarital consultations. Two hundred and fifty-two (50.4 per cent) had been pregnant from one to twelve times and had had 581 pregnancies. Three hundred and fifty-four (60 per cent) were accidental pregnancies and 227 (40 per cent) were planned.

One hundred and eighty-one (71.8 per cent) women had been accidentally pregnant with 354 unplanned pregnancies and 134 (53 per cent) had had 227 planned pregnancies. By comparison there were one-fifth (19 per cent) more women who had accidental pregnancies. Of the 252 women who had been pregnant, 112 (48 per cent) had been pregnant once, sixty-three (25 per cent) twice, thirty-four (13 per cent) three times, twenty-five (9.9 per cent) four times, eight (3 per cent) five times, four (1.5 per cent) six times, five (1.9 per cent) seven times, one (0.4 per cent) eight times, one (0.4 per cent) ten times, and two (0.8 per cent) twelve times.

Of the 368 women married at the time of consultation, 221 (50 per cent) had been pregnant one to twelve times. Of these, 131 (59.3 per cent) of the group of married women had planned pregnancies and 153 (69.2 per cent) had accidental (unwanted) pregnancies. Of the total 134 women who planned 227 pregnancies, sixty-two (46 per cent) planned one pregnancy, fifty-three (39 per cent) planned two pregnancies, fifteen (11 per cent) planned three, two (1.4 per cent) planned four and one (0.7 per cent) planned six. Two hundred and forty-eight (49.6 per cent) of the 500 women had never been pregnant. Of these nulliparous women, 147 (40 per cent) were married at the time of consultation and 101 (76.5 per cent) came premaritally.

Of the 181 women accidentally pregnant, 106 (54 per cent) had one unwanted pregnancy; thirty (16 per cent) had two accidental pregnancies, fourteen (7.8 per cent) had three, thirteen (7.2 per cent) had four, four (2.2 per cent) had five, six (3.3 per cent) had six; two (1.1 per cent) had eight and one each (0.5 per cent) had eleven and twelve.

Three single women were diagnosed as pregnant at first consultation; one two months, one three and one-half months and one five months pregnant. The largest cause for accidental pregnancies in the prematurally

TABLE 10.—*Frequency of Coitus in Marriage*

(Figures Obtained for 177 Cases)

Frequency of Coitus	Before Consultation: Number of Women	Before Consultation: Percentage of Women	After Consultation: Number of Women	After Consultation: Percentage of Women
None	4	2.3	1	0.5
Once a month	4	2.3	6	3.5
Twice a month	6	3.5	2	1.1
Once a week	33	19.0	35	20.0
Twice a week	66	39.0	53	31.0
Three times a week	40	23.0	41	24.0
Four times a week	8	4.6	15	8.9
Five times a week	6	3.5	11	6.5
Daily	10	6.0	8	4.9

TABLE 11.—*Fertility of 500 Women*

(Parity in Married and Premarital * Groups)

Marital Status	Total Number	Nulliparous Women: Number	Nulliparous Women: Per Cent	Multiparous Women—Parity 1-12 Times: Number	Multiparous Women—Parity 1-12 Times: Per Cent	Women with Planned Pregnancies: Number	Women with Planned Pregnancies: Per Cent	Women with Accidental (Unwanted) Pregnancies: Number	Women with Accidental (Unwanted) Pregnancies: Per Cent
Married and unmarried women	500	248	49.6	252	50.4	134	53.0	181	71.8
Married women	368	147	40.0	221	60.0	131	59.3	153	69.2
Premarital women 93 engaged 39 single	132	101	76.5	31	23.5	3	9.7	28	90.3

* The "premarital group were those seen prior to marriage but who after marriage had pregnancies as classified. A small group, twenty-six, 10 per cent of the 252 parous women or 5 per cent of the total group of 500, had been pregnant out of wedlock or truly premaritally.

instructed and single group was condoms breaking, nine cases; next, withdrawal, seven cases; five women used no precautions, three inserted vaginal diaphragms incorrectly, failing to cover the cervix, and two became pregnant using just a douche. In two cases the causes were not known. The contraceptive pessary was not used by any of the unattached women. All of this group were having sexual relations before consultation.

TABLE 12.—*Gravidity Analysis of Women with Planned and Unplanned Pregnancies*

Gravida, Number of Times Pregnant	Women Pregnant 1-12 Times			Women Accidentally Pregnant			Women with Planned Pregnancies		
	Married	Premarital Group	Totals of 500 Women	Married	Premarital Group	Totals of 252 Women with Pregnancy	Married	Premarital Group	Totals
0	147	101	248	..	..	..	..	..	..
1	88	24	112	81	25	106	60	3	63
2	60	3	63	28	2	30	53	..	53
3	33	1	34	13	1	14	15	..	15
4	24	1	25	11	2	13	2	..	2
5	8	...	8	4	..	4	..	..	..
6	4	...	4	6	..	6	1	..	1
7	5	...	5	..	..	..	..	..	..
8	1	...	1	2	..	2	..	..	..
9	...	...	...	..	..	..	..	..	..
10	1	...	1	..	..	..	..	..	..
11	...	...	...	1	..	1	..	..	..
12	2	...	2	1	..	1	..	..	..

TABLE 13.—*Number of Pregnancies, Planned and Unplanned*

	Number of Pregnancies	Number of Accidental Pregnancies	Percentage of Accidental Pregnancies	Number of Planned Pregnancies	Percentage of Planned Pregnancies
Married group....	540	315	58.0	225	42.0
Premarital group	41	39	....	2	....
Totals.....	581	354	60.2	227	39.8

The average size of the family was 1.8 children per mother. Forty-three per cent had one living child, 40 per cent had two children, 11 per cent had three, 2.3 per cent had four, 1.7 per cent had five and 0.5 per cent had eleven. One pair of twins occurred in 314 living births.

In this study the usual family consisted of one or two children; occasionally there were three and exceptionally four or five. There were rarely more than five children.

Planned pregnancies occurred mostly between 21 and 29 years of age, the majority, seventy-six before 25 years. There were ninety-five planned pregnancies before 30, and twenty-two between 30 and 40 years. There was little difference between the ages of the majority of planned and accidental pregnancies, except that more accidental pregnancies occurred between 35 and 45 years of age. There were decidedly fewer unplanned pregnancies in the prematurally instructed group.

Of 252 pregnant women, 106, or 42 per cent, admitted to 151 abortions. Sixty-eight, or 64 per cent, had had one abortion and twenty-two, or 20 per cent, had had two abortions. One admitted to eight abortions.

Comparison of twenty-five criminal abortions after scientific contraception with 127 before indicates the ability of medically prescribed birth control to decrease the number of criminal abortions to one fifth, with subsequent prevention of maternal morbidity and possible sterility. The majority of abortions occurred in married women.

The sexual adjustment of the husband was given as improved in 342 cases after consultation and the same or unimproved in fifty-one cases.

Of ninety engaged couples who came for premarital sex advice, fifty-nine, or 65.5 per cent, of the men had not had sexual experience and thirty-one, or 34.5 per cent had had sex relations. Practically two thirds of the engaged men in this study had remained abstinent until marriage. Forty-one of the 368 women in the married group expressed dissatisfaction with their husband's sexual ability. Three complained of impotence, fifteen of premature ejaculation and twenty-three of inadequate sex relations. The rest complained of the husband's lack of interest in preliminary love play, manual stimulation or selfishness. A few complained of distaste for husbands due to halitosis, unhygienic body care, fear of venereal disease and odious comparisons with other sex partners.

When medical contraceptive advice is not obtained, the man is relied on for assuming contraceptive measures. Three hundred and fifty-six husbands (81 per cent) practiced contraception: by use of condoms alone in 235 cases (52 per cent) and alone or in combination with jelly, suppository or douche in 265 cases (60 per cent), while coitus interruptus was used in ninety-one cases (20 per cent), alone in eighty-six cases and combined with a douche in five cases.

TABLE 14.—*Reasons for Accidental Pregnancies in Single Women and Those Prematurally Instructed*

	Number of Women Accidentally Pregnant			Cause and Number of Times Contraceptive Method Failed					
	Pregnant Once	Pregnant Twice	Pregnant 4 Times	Unknown	Condom Broke	Withdrawal	Douche	Poor Technic Vaginal Diaphragm	Nothing Used
Women with accidental pregnancies after receiving contraceptive advice prematurally (9)	9	..	..	2	2	1	..	3	1
Single (pregnant out of wedlock before consultation [17])	14	2	1	..	7	6	2	..	4
Total number of women (26)	23	2	1	2	9	7	2	3	5

TABLE 15.—*Size of Family*

Total number of women with living children	171
Total number of living children	314
Number of stillbirths	7
Average number of children per mother	1.8

Multiple births—1 pair of twins among 314 living children born to 171 pregnant mothers.

TABLE 16.—*Distribution of Size of Family*

Number of living children per mother	1	2	3	4	5	11
Number of women	74	69	20	4	3	1
Percentage of women	43.0	40.3	11.0	2.3	1.7	0.5

The woman relied on the douche alone and in combination in 90 cases (20 per cent). "Feminine hygiene," or use of contraceptive jellies alone and in combination, was practiced by forty-six (10.5 per cent). Vaginal diaphragms were used by thirty (6.8 per cent), cervical caps by five (1 per cent). Occlusive pessaries were used by only 8 per cent of the women before medical consultation. Fourteen, or 3.2 per cent,

resorted to vaginal suppositories alone or in combination. Only three (6.8 per cent) used the "safe period" and one (0.2 per cent) used lactation. Four (0.8 per cent) practiced abstinence and two (0.4 per cent) had external coitus. Twenty-five (5.7 per cent) used no contraceptive, admitting that they did not want pregnancies but did not understand the process of conception and knew nothing of the possibility for contraception.

TABLE 17.—*Age of Pregnant Women*

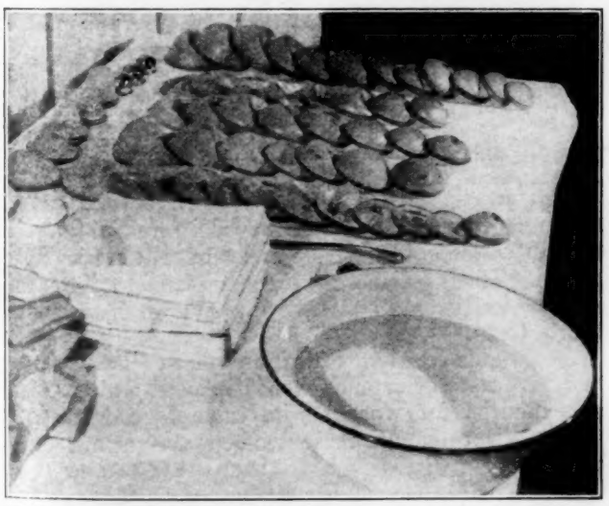
A. Unplanned Pregnancies			B. Planned Pregnancies		
Age	Married Women	Premarital Women	Age	Married Women	Premarital Women
16	2	1	19	7	..
17	3	3	20	10	..
18	6	1	21-25	59	1
19	7	1	26-30	29	1
20	10	4	31-35	21	..
21-25	53	5	36-40	1	..
26-30	33	7			
31-35	29	2			
36-40	5	2			
41-45	3	..			

TABLE 18.—*Pregnancy Wastage (Abortions, All Types)*

							Totals
Number of women	68	22	6	8	1	1	106
Number of abortions	1	2	3	4	7	8	151
Number of unmarried women (engaged or single)	10	..	1	1			

TABLE 19.—*Pregnancy Wastage (Criminal and Therapeutic Abortions)*

	Number of Criminal Abortions	Number of Therapeutic Abortions
Before consultation for contraceptive advice	127	6
After consultation for contraceptive advice	25	7



Types of medically prescribed contraceptive pessaries.

The choice and most frequent medically prescribed contraceptive method was the use of a vaginal type occlusive rubber diaphragm lubricated with a spermacidal jelly or cream. Of the 500 women examined, fifty-three had no method prescribed because of such reasons as sterility, existing pregnancy or operation required for pelvic abnormality. Of the 447 women given birth control advice, 413 (92.3 per cent) were fitted and instructed in the use of rubber occlusive pessaries, 406 (90.8 per cent) vaginal type diaphragms and seven (1.5 per cent) cervical caps. Twenty-six (5.8 per cent) women preferred to have the husband use condoms and seven of these also injected jelly intravaginally before coitus. The modern method places the contraceptive measure in the hands of the wife. The sizes of vaginal diaphragms most frequently used were No. 80 (140 cases), No. 75 (116 cases), No. 85 (sixty-two cases), No. 70 (fifty-four cases), No. 90 (twenty-one cases), No. 65 (seven cases), No. 60 (three cases), No. 95 (two cases) and No. 100 (one case).

The average size of vaginal diaphragm used was No. 80 with No. 75 ranking second and No. 85 in third place. No. 65 or smaller is seldom required, while No. 90 is fairly frequent.

TABLE 20.—*Sexual Experience and Adjustment of Husbands*

	Premarital Sex Experience	No Premarital Sex Experience	Impaired Sex Ability	Premature Ejaculation	Impotence
Husbands of married group	34	?	23	15	3
Male partners in engaged group	31	59	..	..	..

TABLE 21.—*Contraceptive Methods Used by 437 Couples Before Consultation*

	Frequency of Use	
	Number of Cases	Per Cent
A. Contraceptive Methods		
Condom	230	....
Coitus interruptus	86	....
Douche	28	....
Suppository	7	....
Safe period (rhythm theory)	3	....
Nothing	25	....
Gold stem wishbone type pessary	1	....
Vaginal diaphragm (rubber)	30	....
French pessary (cervical type)	2	....
Lanteen pessary	3	....
Contraceptive jelly alone	4	....
Coitus interruptus and douche	5	....
Condom and suppository	3	....
Condom and douche	25	....
Condom and jelly	7	....
External coitus	2	....
Lactation	1	....
Suppository and douche	4	....
Abstinence	4	....
B. Male Methods of Contraception		
Condoms alone and with jelly, suppository or douche	265	60.6
Coitus interruptus alone and with douche	91	20.7
Total male methods	356	81.3
C. Female Methods of Contraception		
Douche alone	28	....
Douche and condom	25	....
Douche and coitus interruptus	5	....
Douche and suppository	4	....
Douche and diaphragm	30	....
Total douche alone and in combination	92	20.0
Vaginal diaphragm	30	6.8
Cervical type pessaries	5	....
Stem pessaries (intracervical)	1	....
Jelly alone	4	....
Jelly with diaphragm	30	....
Jelly with cervical type pessaries	5	....
Jelly with condoms	7	....
Total jelly alone and in combination	46	10.5
Suppositories alone	7	....
Suppositories and condom	3	....
Suppositories and douche	4	....
Total suppositories alone and in combination	14	3.2
Safe period	3	0.68
Lactation	1	0.2
D. Other methods		
External coitus	2	0.4
Abstinence	4	0.8
Nothing used (pregnancy not desired)	25	5.7

(The vaginal diaphragm extends from behind the symphysis pubis along the anterior vaginal wall to the posterior fornix behind the cervix, not serving just as a cervical cap.)

Where anatomic reasons preclude fitting with vaginal diaphragms, a cervical type is prescribed. This is a suction cap covering just the cervix, also lubricated with contraceptive jelly or cream. (Cervical types are more difficult to place and easier to dislodge. Careful technic is required.)

When no type of occlusive pessary can be fitted, or when the woman refuses to use one, the only other reliable method is the use of the condom. With proper technic and instruction this method is highly reliable but has many disadvantages which the diaphragm method overcomes.

Disadvantages of the condom method are:

1. Many husbands cannot or will not use condoms.
2. Lack of knowledge of testing and proper use are responsible for frequent failure due to breaking, leaking or the condom slipping off.
3. Chemical preservatives or nonlubrication causes irritation to male and female genitals.
4. Physiologically it is difficult for some women to reach orgasm before the husband ejaculates; the condom prevents a normal female climax.
5. It is psychologically undesirable to some men and women, as it interrupts love play.
6. It diminishes sensation for both partners.
7. It is more expensive than the pessary method.

One woman had four failures. Another wife conceived extramaritally thinking she was sterile; her husband was found to be sterile.

There were 180 cases of failure reported due to: (1) condoms, seventy-two cases (40 per cent); (2) withdrawal, forty-three cases (23.8 per cent); (3) douche alone, twenty-four cases (13.3 per cent); (4) nothing used, sixteen cases (8.8 per cent); (5) vaginal diaphragm, ten cases (5.5 per cent); (6) vaginal suppositories, eight cases (4.4 per cent); (7) contraceptive jelly alone, three cases (1.6 per cent); (8) cervical pessaries, two cases (1.1 per cent); (9) gold stem wishbone pessary, one case; (10) believed herself sterile, one case (0.5 per cent).

Use of vaginal diaphragms was 97.6 per cent successful as a contraceptive method. It was the most efficient method that was used. The causes for failure were due to human elements, either improper fitting and improper type prescribed or improper use, careless technic or lack of use. There was no case of unexplained failure. No sterility was caused by use of an occlusive diaphragm or cervical cap.

Acute gonorrhea was diagnosed in seventeen women and two cases of syphilis were disclosed and treatment was advised for women who came for contraceptive advice. Not one of these women was aware of the nature of her disease.

TABLE 22.—*Medically Prescribed Contraceptive Methods*

Contraceptive Methods	Number of Cases	
Vaginal diaphragms (rubber, coiled and watch spring rims) with spermacidal jelly or cream	406	
Cervical type occlusive pessary	7	
(*a*) Dumas	3	
(*b*) Mizpah	4	
Total occlusive pessaries		413
Condoms alone	19	
Condoms with jelly	7	
Total use of condoms		26
No method prescribed		53

TABLE 23.—*Sizes of Vaginal Diaphragms Prescribed*

Sizes (Mm.)	Number Prescribed
60.0	3
65.0	7
70.0	54
72.5	22
75.0	94
77.5	27
80.0	113
82.5	12
85.0	50
87.5	2
90.0	19
95.0	2
100.0	1

TABLE 24.—*Number of Women Using Contraceptive Methods Successfully and Time of Use*

(All Types—No Unplanned Pregnancies)

Time	Number of Women
From 1 to 6 months	13
6 to 12 months	21
12 to 17 months	71
18 to 24 months	71
2 to 3 years	57
3 to 4 years	47
5 to 9 years	79
10 to 14 years	48
15 to 19 years	27
20 to 24 years	12
25 to 30 years	5

TABLE 25.—*Causes of Failure of Contraceptive Methods*

(All Types—180 Cases Reported)

Method Used Which Failed	Number of Women with Unwanted Pregnancies
Condoms	72
Withdrawal	43
Douche	24
Nothing used	16
Vaginal diaphragm	10
Vaginal suppositories	8
Vaginal jelly alone	3
Cervical pessaries	2
Gold stem pessaries	1

TABLE 26.—*Analysis of Ten Vaginal Diaphragm Failures*

(413 diaphragms used, 36 fitted elsewhere—2.4 per cent failures)

Reasons for failures

1. Poor technic in application; inserted into anterior fornix (cervix uncovered)
2. Failure to feel the cervix covered
3. Immediate removal after use without a douche
4. Improper fitting; wrong size or type
5. Acknowledged omission of diaphragm on occasion; "took a chance"
6. Discontinued use; lazy, too much trouble
7. Inserted only at end of coitus
8. Lanteen type used without fitting or instruction or fitting
9. Used same size without refitting after delivery (required larger size)
10. Purchased diaphragm in drug store and used without instruction

SUMMARY

A study of 500 private contraceptive cases is presented, in 94.3 per cent of which contraception was admittedly being practiced before the medical consultation. The cases are drawn from various religious, age and economic groups. The women requested contraceptive advice for a variety of health, psychologic and economic reasons. More than 50 per cent (276) of the women in this study were employed of necessity. Ninety per cent of the "premarital" group stated that they had

to continue working after marriage. Half of the group of 500 stated that inadequate income was their main reason for wanting to avoid further pregnancies.

The majority of women sought contraceptive advice during the first year of marriage, the remainder from one to thirty years after marriage. The trend among the younger group is toward obtaining contraceptive advice premaritally.

Fifty-seven per cent of the unmarried and 6.5 per cent of the married women had intact hymens. Most of these required medical dilation. Thirty-eight per cent of those seeking premarital advice were already having sex relations.

Fifty-three per cent of the women had planned pregnancies, usually one or two children, the average being 1.8 children per mother. Of all the pregnancies, 60 per cent were accidental and resulted from the failure of various types of contraception. An analysis of these failures is given. Five per cent of the total group had been pregnant before marriage. Very few accidental pregnancies occurred in the group instructed premaritally.

TABLE 27.—*Reasons Patients Discontinued Use of Any Contraceptive*

(96 cases reported)	Number of Cases
1. Planned pregnancies	24
2. Pregnancy diagnosed first visit (accidentally pregnant)	38
3. Female sterility (diagnosed by Rubin test, operation, laboratory reports)	17
(*a*) Closed tubes	4
(*b*) Fibroids or hysterectomy	9
(*c*) Oophorectomy	2
(*d*) Menopause	2
4. Wife erroneously believed herself sterile	1
5. Male sterility	4
(*a*) Undescended testicles	1
(*b*) Impotence	2
(*c*) Husband insane	1
6. Divorced, separated, widowed, terminated sex relations	10
7. Laziness	2

TABLE 28.—*Menstruation—Types and Character*

Type	Number of Cases
Regular (28-32 day cycle)	407
Irregular	89
Dysmenorrhea (severe)	95

TABLE 29.—*Pelvic Abnormality Found on Routine Pelvic Examination for Fitting Diaphragms*

Pathologic State	Number of Cases
Pregnant on examination	38
History of oophorectomy and salpingectomy	7
Retroversion	105
Cervical erosion	142
Adnexitis	54
Badly lacerated cervix	64
Fibroid uterus	43
Ovarian cysts	39
Large cystocele-rectocele	27
Cervical polyps	7
Septate hymen	2
Acute gonorrhea	17
Vaginitis (trichomonas)	15
Clitoral adhesions	2

A most important observation was that medically prescribed contraceptive advice reduced the number of abortions by four fifths. Forty-two per cent of the 252 parous women had had abortions. Sixty-four per cent admitted to one abortion and 36 per cent had had two or more abortions. The majority of abortions occurred in married women.

Before medical consultation 81 per cent of the husbands practiced contraception by the use of condoms or coitus interruptus and 20 per cent of the women used a douche.

The most frequent method which I prescribed was the vaginal diaphragm lubricated with a contraceptive jelly

TABLE 30.—*Venereal Disease Statistics*

	Gonorrhea	Syphilis
Number of husbands	0	1
Number of wives	17	2

TABLE 31.—*Summary of Causes for Sexual and Marital Dissatisfaction*

Reasons	Number of Wives
1. Fear of consequences of repeated abortions	120
2. Fear of unwanted pregnancy	229
3. Faulty contraceptive methods (inadequate opportunity for orgasm)	54
4. Dyspareunia (vaginismus, improper sex technic)	42
5. Fear of coitus	229
6. Ignorance of reproductive process and genital anatomy	24
7. Emotional frustration due to sterility	16
8. Aversion to coitus (frigidity)	37
9. No sex desire (low basal metabolism rate found)	9
10. Anatomic causes for unsatisfactory coitus	16
(*a*) Tight resistent septate hymen	
(*b*) Size and location of clitoris	
(*c*) Extreme obesity of either husband or wife	
(*d*) Infantile genital development	
(*e*) Pelvic abnormality, e. g. parametritis, torn perineum, retroversion	
(*f*) Irritating vaginal discharges	
(*g*) Dyspareunia	
11. Disparity in age	4
12. Venereal disease	6
13. Infidelity	5
14. Secret use of contraceptive by wife	2
15. Masturbation preferred to coitus	4
Other frequent complaints:	
16. Male sex inadequacy	
17. Prolonged debilitating illness of one partner	
18. Anxiety over economic insecurity (husband unemployed, wife sole wage earner)	
19. Manual clitoral stimulation preferred to coitus	
20. Too frequent pregnancies	
21. Cultural aesthetic inequalities	
22. Lack of privacy (poor housing)	
23. Husband's preference for perversions	
24. Faulty attitude of husband or wife toward normal sex and marriage intimacies	

or cream (90.8 per cent of the cases). The sizes most frequently prescribed were, in order, 80 mm., 75 mm. and 85 mm. This method proved to be 97.6 per cent effective and improved marital adjustment. The most frequent causes for sexual dissatisfaction are analyzed.

Every "premarital" couple expressed the desire for offspring in the future. They felt the need for temporary contraceptive advice and wanted the assurance that the method would not cause sterility.

Contraception is a health problem of importance both to the patient and to the physician and involves the welfare not only of the individual but also of society.

20 West Eighty-Sixth Street.

Schizophrenic Thinking.—The peculiar qualities of schizophrenic thinking and behavior generally are dependent principally on four conditions: (1) the schizophrenic turns away from reality (introversion); (2) his thinking is dominated by his complexes (topics with a strong affective coloring) to an extent not seen in the normal; (3) he regresses to a childish or infantile or archaic mode of thought, and (4) his personality undergoes a progressive distintegration. These are not separate and distinct conditions but different aspects of one and the same thing.—Henderson, D. K., and Gillespie, R. D.: A Text-Book of Psychiatry for Students and Practitioners, London, Oxford University Press, 1940.

BLOOD SUGAR STUDIES ON GOLFERS

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Most sugar tolerance tests are performed on patients fasting and at rest, although many interesting studies have been made on persons during and after exercise.

The effects of exercise on blood sugar were first reported by Chaveau and Kaufmann.[1] They demonstrated as far back as 1886 that the blood sugar in a vein leading from the masseter muscle of a horse decreased on chewing. Weiland [1] in 1908 showed that venous blood sugar concentration was lower after exhausting exercise. In 1924 Levine, Gordon and Derick [2] showed that blood sugar levels decreased appreciably following exercise. Their studies were based on a group of runners who participated in the American marathon race of 25 miles in Boston, April 19, 1924. Working on the same general group of runners one year later, Gordon, Kohn and Levine [3] demonstrated that the lowest blood sugar levels were found between the fourteenth and eighteenth miles. Those runners who were sustained during the race on a high sugar intake were much less fatigued than those who were not and performed better generally. Wollmer [4] reported an immediate rise in blood sugar after exercise, followed

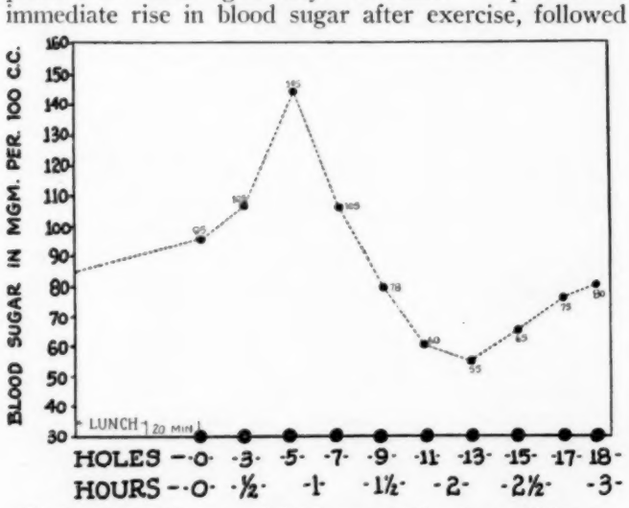

Chart 1.—Composite curve of blood sugar readings in a golf foursome taking three hours to complete. A definite drop begins at the ninth hole, reaching its lowest level at the thirteenth.

by a decline. He compared normal and obese subjects and found no appreciable difference in the two. Best and Partridge [5] in their studies on Olympic athletes in 1928 described a depression in blood sugar levels following intense exercise. Strandell [6] in 1934 and Boje [7] in 1937 showed comparable manifestations among persons subject to measured amounts of exercise. The Smiths [8] in 1937 demonstrated similar falls in normal individuals, but more pronounced drops in blood sugar in diabetic patients following exercise. It was felt, therefore that studies should be undertaken on a sport played by a comparatively large number of people, namely golf, with the hope of evaluating some data which may be of practical use. There are at the present time over two million golfers [9] playing on three thousand courses in the United States. Assuming that the greatest number of American golfers have handicaps ranging from 10 to 27, thirty subjects for the following experiment were taken from that group. They ranged from 35 to 45 years in age and were apparently healthy males with no evidence of diabetes. As far as possible these studies were performed under their normal playing conditions. They were allowed to eat their usual luncheons and played afternoon rounds of golf under normal conditions with the exception that they were not permitted to smoke during the tests. Blood sugar estimations were taken before and after lunch. (The tests were done by the Folin-Wu method on venous blood.) Thereafter blood specimens were taken at every odd numbered hole for the entire round. A composite average curve may be seen in chart 1. The postprandial rise reached its maximum at the fifth hole. At the seventh hole the blood sugar was down to 105 mg. per hundred cubic centimeters. From the eleventh to the fifteenth it was well below fasting. At the seventeenth hole it was almost back to the fasting, at which point it was carried on to the end, with a slight rise at the eighteenth hole. Chart 1 is the curve of an average foursome taking approximately three hours to complete. This curve is somewhat changed in a twosome, as the time element naturally influences the reaction (chart 2).

COMMENT

The lowest blood sugar readings were observed between the ninth and fifteenth holes in the case of a foursome and between the eleventh and the fifteenth in the case of a twosome. This period coincides with the time when the subjects complained mostly of fatigue. It was also during this period that the greatest number of poor shots were made by the golfers and the scores were the highest. The poorer golfers showed lower blood sugar curves in many instances because of the fact that they expended more energy in playing the game and showed greater signs of exhaustion. They also showed more evidence of mental and emotional fatigue as a result of their anxiety. This was probably part of a vicious circle, one factor influencing the other. The more high strung and excitable the subject, the more intense the mental fatigue. The more composed and accomplished golfers had fewer mental or physical changes during this period of hypoglycemia and their blood sugar did not descend to such low levels. In explaining this phenomenon two factors must be considered. The first is fatigue and the second anxiety,[10] and the two are closely interrelated.

Muscular exercise results in the conversion of glycogen into lactic acid, one fifth of which is converted into carbon dioxide and water (glycolysis), but most of the remaining is reconverted into glycogen. In the liver, lactic acid is changed into glycogen, in which form it may be stored or liberated as dextrose into the blood stream. Glycogenesis in the liver is affected directly by the action of the pancreas (insulin). An increase in the utilization of dextrose by exercise is followed by an increase in hepatic glycogenolysis. In anxiety states there is probably an increase in the production of

1. Quoted by Strandell, B.
2. Levine, S. A.; Gordon, Burgess, and Derick, C. L.: Changes in Chemical Constituents of Blood Following a Marathon Race, J. A. M. A. **82**: 1778 (May 31) 1924.
3. Gordon, Burgess; Kohn, L. A.; Levine, S. A.; Matton, Marcel; Scriver, W. de M., and Whiting, W. B.: Sugar Content of Blood in Runners Following a Marathon Race, with Especial Reference to the Prevention of Hypoglycemia: Further Observations, J. A. M. A. **85**: 508 (Aug. 15) 1925.
4. Wollmer, M.: Blutzuckerspiegel und Muskerlarbeit bei Gesunden und Fettsuchtigen, Deutsches Arch. f. klin. Med. **170**: 122, 1931.
5. Best C. H., and Partridge, R. C.: Observations on Olympic Athletes, Proc. Roy. Soc. s. B. **105**: 323 (Sept. 2) 1929.
6. Strandell, B.: On the Influence of Exercise on the Blood Sugar, Especially in Connection with Dextrose Ingestion, Acta. med. Scandinav. supp. 55, p. 1, 1934.
7. Boje, O.: Die Restredaktion des Blutes in der Ruhe und Wahrend korperlicher Arbeit. Skand. Arch. f. Physiol. supp. 9, 11.
8. Smith, F. H., and Smith, K. A.: The Influence of Muscular Exercise on Blood Sugar Concentrations, J. Clin. Investigation **16**: 289 (May) 1937.
9. Personal communication from the Professional Golfers Association.
10. Quinlan, John F.: Hypoglycemia in Relation to the Anxiety States and the Degenerative Diseases, California & West. Med. **49**: 446 (Dec.) 1938.

epinephrine, which results in the acceleration of glycogenolysis in all cells. The glycogen content of muscles decreased appreciably during the action of epinephrine. Thus this combined action of exercise and anxiety results in first a definite increase in blood sugar, followed by a decided fall, resulting in part from an increased liberation of insulin. The latter activity in a foursome coincides therefore with the hypoglycemic symptoms experienced during the period between the ninth and fifteenth holes, or between one and one-half hours and two and one-half hours, and in a twosome between the eleventh and fifteenth holes. The return in the later holes to normal figures is due to glycogenolytic activity of the liver with liberation of dextrose into the blood stream, aided in part by increased hydrogen ion concentration. Studies of metabolic activities of a parallel nature were not performed but it would be interesting to speculate as to the decrease in serum phosphate during this period of blood dextrose depression, as well as lactic acid increase, with correlation of blood pressure readings as well.

From a practical point of view, two suggestions may be made to help combat this period of hypoglycemia: first, a more ketogenic type of lunch, and second, increased carbohydrate intake in the form of sugar or

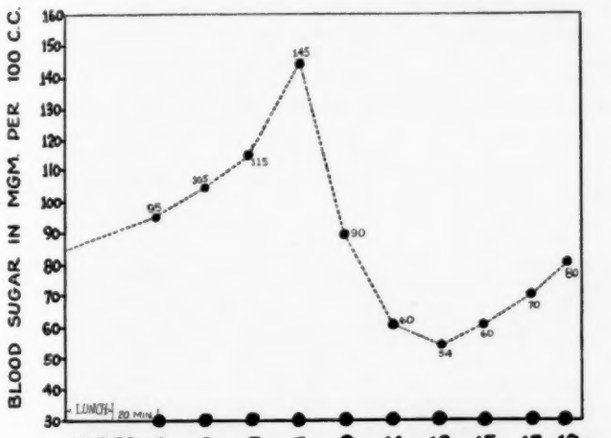

Chart 2.—Composite curve of blood sugar readings in a golf twosome taking two and a half hours to complete. There is an elapsed time of twenty minutes between the end of lunch and starting play.

candy near the eighth hole in a foursome and the ninth hole in a twosome. Following such a regimen, blood sugar levels did not reach such low figures and the players showed fewer signs of fatigue throughout the match.

SUMMARY

Blood sugar studies were made on thirty male golfers ranging from 30 to 45 years of age and possessing handicaps of from 10 to 27.

Following usual luncheons and playing under ordinary conditions, blood sugar dropped to hypoglycemic levels between the ninth and fifteenth holes in a foursome, and between the eleventh and fifteenth holes in a twosome. These periods corresponded to the time of lessened efficiency of the players.

These observations were more pronounced in the more nervous and less accomplished golfers, and less marked in the more able and poised golfers.

More ketogenic types of lunch and consumption of sugar or candy at the seventh or ninth hole resulted in definite decrease in untoward symptoms and, on the whole, better scores.

434 Thirteenth Street.

Clinical Notes, Suggestions and New Instruments

CYCLIC PULMONARY EDEMA AT MENSES IN MITRAL STENOSIS

RELIEF FOLLOWING IRRADIATION OF PITUITARY GLAND

JOSEPH EDEIKEN, M.D., AND JOHN Q. GRIFFITH JR., M.D.
PHILADELPHIA

Acute pulmonary edema in mitral stenosis is not infrequent and may be precipitated by a number of factors. Retention of fluid during the menses is well known and may, among other causes, be due to overactivity of the antidiuretic hormone of the posterior lobe of the pituitary gland. In the vast majority of cases there are few resultant phenomena except an increase in body weight. In the case to be reported, however, advanced mitral stenosis was associated with a marked decrease in cardiac reserve, and serious pulmonary symptoms occurred in each of seventeen successive menstrual periods. Blood studies strongly suggested overactivity of the posterior lobe of the pituitary gland, and the subsequent relief afforded by irradiation of the pituitary gland supports this hypothesis. As far as we are able to determine, no case of a similar nature has been reported in the literature.

REPORT OF CASE

Mrs. B. G., aged 26, was in good health except for slight dyspnea on exertion until the night of Dec. 31, 1937, when while dancing she experienced a feeling of tightness in the chest and throat, a hacking cough and a sense of suffocation. This was followed by a gurgling in the chest and throat which was audible to her husband. The attack lasted until noon the next day and was finally relieved by morphine and inhalations of oxygen. However, the same episode was repeated during the following two days. After several weeks of comparative good health she suffered a series of similar attacks. All the attacks except the initial one occurred at rest and usually during sleep. It was then noted that the attacks occurred only in association with her menstrual period, either immediately preceding the onset or during the period, although they occasionally continued a day or two after the cessation of the flow. Her periods were regular and of normal duration and flow.

She was seen by one of us (J. E.) Nov. 19, 1938, in an attack of acute pulmonary edema with a history of having been awakened from sleep by the symptoms just described. Examination was difficult because of extreme restlessness and cough. Cyanosis was marked, loud bubbling rales were heard throughout the chest, and the heart was extremely rapid, with the typical manifestations of mitral stenosis. The blood pressure was 110 systolic, 80 diastolic. The attack was controlled by two doses of morphine sulfate, each one-fourth grain (0.016 Gm.), within one hour, but the attacks recurred during the next two days. She was admitted to the Mount Sinai Hospital in Philadelphia on November 22, but no further attacks occurred. A blood count showed 82 per cent hemoglobin, 4,280,000 red blood cells and 11,600 white blood cells, of which 70 per cent were polymorphonuclear leukocytes. Except for blood probably incident to menstruation, the urine was normal; blood sugar was 90 mg. and urea 19 mg. per hundred cubic centimeters of blood. The Wassermann reaction was negative. The basal metabolism reading was —11 per cent. The illustrations show the electrocardiogram and the orthodiagram done November 23.

According to the patient and her family, a murmur was heard on routine examination when she was pregnant in 1935, but the lesion was evidently not considered a serious one as activities were not restricted and cardiac studies were not done. There was no history of rheumatic fever, chorea, scarlet fever or repeated attacks of tonsillitis.

In spite of full digitalization, the same violent recurring attacks of pulmonary edema took place at subsequent periods, each requiring one-half grain (0.032 Gm.) of morphine sulfate for relief. Examination of the urine for estrogenic substances

Dr. Griffith is Atwater Kent Fellow in Medicine.
From the Edward B. Robinette Foundation, Medical Clinic, of the Hospital of the University of Pennsylvania.

by Dr. Charles Mazer just before the onset of the period in January 1939 showed 3.3 rat units of active estrogen and 6.6 rat units of combined and active estrogen, or about one-fifth the amount usually found premenstrually. Purely from a substitutive standpoint large doses of progynon were given by intramuscular injection, but in February the usual attack of pulmonary edema initiated her period. Because of the possibility that increased blood volume due to water retention incident to menstruation might be a factor in the production of the attack, mercupurin 2 cc. intravenously was given in addition to the morphine. There was a profuse diuresis and, unlike the preceding periods, pulmonary edema did not recur in the succeeding days of this period. The conception of increased blood volume during the menstrual period was subsequently confirmed by blood volume determinations done by one of us (J. Q. G.). On March 16, 1939, the blood volume, measured by the method of Sunderman and Austin, was 65 cc. per kilogram of body weight and the melanophore expansion test was negative. Her serum contained no antidiuretic substance for rats. On March 30, during her menstrual period, the blood volume rose to 78 cc. per kilogram of body weight, the melanophore expansion test was positive and her serum contained an antidiuretic substance for rats.

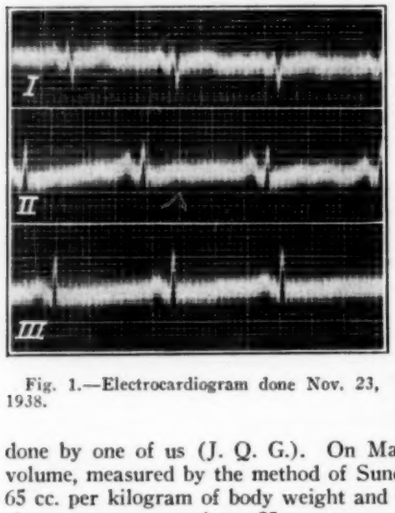

Fig. 1.—Electrocardiogram done Nov. 23, 1938.

The increase in blood volume and the positive rat and frog tests suggested the possibility of overactivity of the pituitary gland. Irradiation of the pituitary gland in an effort to diminish its antidiuretic effect was suggested, but the patient refused. Castration by means of x-rays or radium was also refused. X-ray examination of the sella turcica was negative.

Thereafter mercupurin was given at approximately weekly intervals but efforts were especially made to give it just before or at the onset of the period. Results were gratifying in that severe attacks of pulmonary edema did not occur, but the patient continued to have a tight feeling in the chest with a hacking cough during her periods. These symptoms were comparatively mild and did not incapacitate her. Several mild attacks of pulmonary edema in the intermenstrual period followed severe exertion, excitement or acute bronchitis.

On June 1 she suffered an attack of pulmonary edema. The menstrual period expected on May 24 was delayed and she had been to a rather hilarious party on the night of May 31. However, she felt well until about 8 p. m. of June 1, when she suffered the severe attack of pulmonary edema. The last dose of mercupurin had been given May 23. This attack was relieved by the usual methods, and menstruation started June 2.

Following this attack the patient consented to have irradiation of the pituitary gland, and 1,132 roentgens was given in eight doses by Dr. Louis Edeiken.

Because the patient was spending the summer at the seashore, injections of mercupurin were continued as a precautionary measure. The menstrual period in July was uneventful and the usual mild symptoms of tightness of the chest and cough were absent. For the first time in seventeen months the patient had not experienced pulmonary symptoms during her period. The menstrual period in August was also uneventful. On returning home in September, the injections of mercupurin were discontinued but the menstrual periods of September, October and November passed without any signs or symptoms of pulmonary congestion. The melanophore expansion test done November 28, the second day of her period, was positive, but the serum contained no antidiuretic substance for rats.

The patient had no further attacks of pulmonary edema but developed mesenteric embolism during an attack of paroxysmal auricular fibrillation on July 6, 1940, and died on July 7.

THE MELANOPHORE EXPANSION TEST

The test as performed for melanophore expanding substance in the blood is as follows: Two frogs of light, well matched color (Rana pipiens) are placed in water near a window until the colors are stationary. It is decided which frog is the lighter of the two, and this frog is injected under the skin of the back with 1 cc. of the serum to be tested. The frogs are then watched over a period of twenty minutes. In a positive test the injected frog darkens definitely as contrasted with the control frog.

RAT TEST FOR POSTERIOR PITUITARY OR POSTERIOR PITUITARY-LIKE SUBSTANCE

The rat test for posterior pituitary or posterior pituitary-like substance in the serum is as follows: Adult rats are taken from the cage where dried food and water have been available as desired. Thus they are presumably neither dehydrated nor hydrated. Without anesthesia they are then given 5 per cent of their body weight of water by stomach tube. Immediately thereafter 1 cc. of the serum of the patient to be tested is injected intraperitoneally. The animals are then placed in metabolic cages and the urine passed over one and one-half hours is measured. Complete voiding is insured at the end of the period by beginning the induction of ether anesthesia in the metabolic cage. Under ether anesthesia blood pressure is measured by the indirect method of Griffith. Three animals are used for each test. A rat given normal serum will excrete under the conditions of the experiment about 40 per cent of the ingested water in the form of urine. This allows for a slight but fairly constant loss in the collecting apparatus. After the procedure the blood pressure will not exceed 140 mm. of mercury. A test is considered positive if at least two of the animals excrete less than 10 per cent of the ingested fluid or if one or more develops a definite hypertension.

COMMENT

Generalized or local edema associated with the menstrual periods of normal women has been reported by a number of observers. Heilig [1] and Petersen and Milles [2] presented evidence to indicate a disturbance of water metabolism associated with the menstrual cycle. The Thorns and Nelson [3] observed a gain in weight of 2½ pounds (1,000 Gm.) or more in twenty-four of fifty normal women during the premenstrual period. These investigators demonstrated a retention of sodium, chloride and water during the premenstrual period and intermenstrual periods and an increase in estrogenic substances in the urine during the periods of sodium and chloride retention. No such studies were made on our patient, and the only evidence suggesting water retention is the increase in blood volume noted on the first day of the menstrual period. The single determination of estrogenic substances in the urine premenstrually showed a decrease rather than an increase. It is possible, however, that another mechanism may play a role, for, as Taylor and his associates [4] remark, "the manner in which estrogens or progesterone may act to prevent sodium excretion can only be guessed at. They may displace sodium into the tissues,

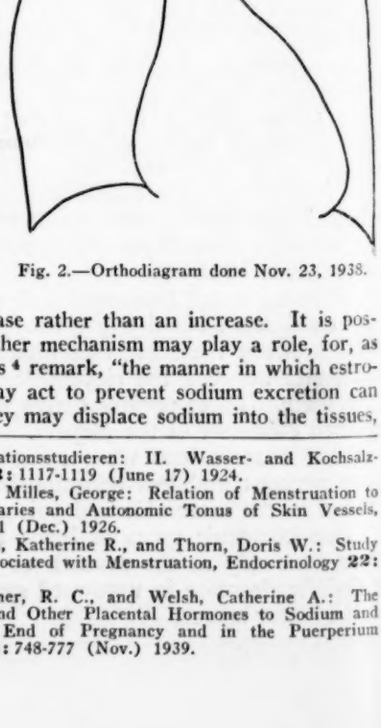

Fig. 2.—Orthodiagram done Nov. 23, 1938.

1. Heilig, R.: Menstruationsstudieren: II. Wasser- and Kochsalzhaushalt, Klin. Wchnschr. **3**: 1117-1119 (June 17) 1924.

2. Petersen, W. F., and Milles, George: Relation of Menstruation to Permeability of Skin Capillaries and Autonomic Tonus of Skin Vessels, Arch. Int. Med. **38**: 663-681 (Dec.) 1926.

3. Thorn, G. W.; Nelson, Katherine R., and Thorn, Doris W.: Study of Mechanism of Edema Associated with Menstruation, Endocrinology **22**: 155-163 (Feb.) 1938.

4. Taylor, H. C.; Warner, R. C., and Welsh, Catherine A.: The Relationship of Estrogens and Other Placental Hormones to Sodium and Potassium Balance at the End of Pregnancy and in the Puerperium Am. J. Obst. & Gynec. **38**: 748-777 (Nov.) 1939.

prevent its excretion by the kidneys, or act through some other gland, as for example the posterior pituitary." In an investigation of water metabolism of fully matured female pig-tailed macaques whose menstrual cycles varied slightly around a mean of approximately thirty days, Krohn and Zuckerman [5] noted that the sexual skin of the animal regularly began to swell during menstruation, resorption of the swelling beginning as a rule shortly before the middle of the cycle. The animal's weight fluctuated with the state of the sexual skin and in one case the increase in weight was as much as 18 per cent.

The antidiuretic effect of the posterior lobe of the pituitary gland has been demonstrated in animals. Experimental evidence indicates that the hormone of the posterior lobe of the pituitary gland causes an increased absorption of fluid in the tubules of the kidney and, according to Peters,[6] the hemodilution that follows ingestion of fluid is exaggerated by solution of posterior pituitary. According to this author the presence or absence of this hormone effects transformations in the elimination as well as in the quantity of urine. Clinically this effect is seen most conclusively in the manner in which solution of posterior pituitary or pitressin checks the functional disturbance of diabetes insipidus.

It is logical to suppose that under certain circumstances the active principle of the posterior lobe of the pituitary gland may be temporarily or permanently increased or decreased. It is claimed by some that lesions of the posterior lobe of the pituitary gland and adjacent portions of the midbrain may cause diabetes insipidus. Conversely, an increased secretion may cause oliguria, as in the patient of Grassheim [7] with a cystic tumor in the midbrain, in whom the oliguria was relieved by operation. The contents of the cyst, when injected into dogs, had an antidiuretic effect.

In our case the available evidence and mode of relief suggests temporary overactivity of the posterior lobe of the pituitary gland at each menstrual period, with resulting antidiuresis, hemodilution and therefore increased blood volume and, because of the advanced grade of mitral stenosis, pulmonary edema. This is purely speculative, but the increase of blood volume during the menstrual periods and the results following irradiation of the pituitary gland suggest the possibility of the aforementioned sequence of events. Unfortunately, because of lack of cooperation on the part of the patient, records of daily weight and urinary output are not available.

In an effort to demonstrate overactivity of the posterior lobe of the pituitary gland, the melanophore expansion test for frogs and tests for antidiuretic substance for rats in the serum of the patient were performed. In studies as yet unpublished, Griffith, Corbit, Rutherford and Roberts [8] were able to produce antidiuresis and, in about a third of the animals, hypertension by giving rats 5 per cent of their body weight of water by mouth along with an intraperitoneal injection of 0.12 cc. per hundred grams of body weight of pitressin [9] diluted 1:150. Hypertension was found not to occur if either the pitressin or the water was given alone. In the technic here recorded 1 cc. of the patient's serum was substituted for the pitressin with essentially similar results. This, of course, does not prove that the substance in the serum was posterior pituitary hormone, but such an explanation appears likely in view of the presence of melanophore expanding substance and the effect of irradiation.

SUMMARY

1. Cyclic pulmonary edema was associated with the menstrual periods of a young woman with advanced mitral stenosis.

2. Repeated attacks of pulmonary edema occurred during fourteen successive menstrual periods. Mercupurin given intravenously during an attack of pulmonary edema prevented subsequent attacks during that period.

3. Injections of mercupurin intravenously, given before the menstrual period, prevented pulmonary edema during three periods, but a hacking cough and tightness of the chest occurred.

4. The patient became entirely free from pulmonary symptoms following irradiation of the pituitary gland and has remained free to date (April 18, 1940), ten months after irradiation).

5. Irradiation of the pituitary was done because examination of the blood the first day of one of the periods showed an increased blood volume and the serum contained an antidiuretic substance for rats and a melanophore expanding substance for frogs.

6. Six months after irradiation of the pituitary gland the melanophore expansion test remained positive but the serum contained no antidiuretic substance for rats.

5. Krohn, P. L., and Zuckerman, S.: Water Metabolism in Relation to Menstrual Cycle, J. Physiol. **88:** 369-387 (Jan. 18) 1937.

6. Peters, J. P.: Body Water, Springfield, Ill., Charles C. Thomas, Publisher, 1935.

7. Grassheim, K.: Wasser- und Kochsalzstoffwechsel beeinflussende Stoffe im Liquor bei Erkrankungen des hypophysaren Systems, Klin. Wchnschr. **11:** 1257-1260 (July 23) 1932.

8. Griffith, J. Q.; Corbit, H.; Rutherford, R. B., and Roberts, E.: Unpublished observations.

9. Each cubic centimeter of pitressin (Parke, Davis & Co.) contains 20 pressor units.

CASE OF ACUTE POISONING FROM DILANTIN SODIUM WITH RECOVERY

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Because the complete pharmacology and toxicology of dilantin sodium, recently introduced for the treatment of epilepsy, are still unknown and because there is, as yet, a paucity of reports of acute poisoning from the drug, the following case is recorded.

Dilantin sodium was introduced as an anticonvulsant by Merritt and Putnam [1] and has been reported on by many investigators. The structure of dilantin sodium (sodium diphenyl hydantoinate) is analogous to that of the barbiturates but it is a derivative of glycolyl urea instead of malonyl urea. The mode of action and the intermediate metabolism and excretion are not yet known. The mild toxic effects produced in some cases by poorly tolerated doses of dilantin sodium can be divided into two groups.[2] The first group is common to phenobarbital and to dilantin sodium and consists of lethargy, ataxia, anorexia, nystagmus and tremor; the second group is characteristic for toxic doses of dilantin sodium and consists of epigastric distress, ocular pain, diplopia, blurred vision and gingival hyperplasia. More serious toxic effects are dermatitis (erythematous, scarlatiniform, morbilliform, exfoliative) and purpuric reactions.

REPORT OF CASE

G. B., a white man aged 25, had epilepsy which resulted from a previous head trauma. His birth and developmental histories were not remarkable. The only illness of note was a severe diphtheritic infection with delirium at the age of 6 years. The family history was negative for neuropsychiatric conditions. At the age of 8 years, when he was running behind a baseball player, he was struck by the baseball bat and rendered unconscious for one hour. He recovered without requiring further care. Since this injury he has had periodic attacks of bifrontal headaches, more marked on the left side. The headaches, unaccompanied by ocular or gastrointestinal phenomena, recur about every three weeks and last all day, unless terminated by acetylsalicylic acid from 10 to 20 grains (0.65 to 1.3 Gm.). His first convulsion occurred nine years after the head injury, when he was 17 years old. Thereafter generalized convulsions recurred at intervals of from six days to four months, despite his taking one-half grain (0.03 Gm.) of phenobarbital three times daily. Because of this complaint he was seen in the outpatient department of the Monson State Hospital May 16, 1939. At this time he had had epilepsy for eight years, the seizures occurring without aura, without any jacksonian features and usually soon after he awakened or with excitement.

The patient was well developed. He was oriented in all spheres, rational, coherent and showed no evidence of hallucinations, delusions or illusions.

The lateral borders of the tongue were scarred. The neurologic and general physical examination were within normal

From the Outpatient Clinic, Monson State Hospital.

1. Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in Treatment of Convulsive Disorders, J. A. M. A. **111:** 1068-1073 (Sept. 17) 1938; Sodium Diphenyl Hydantoinate in Treatment of Convulsive Seizures Arch. Neurol. & Psychiat. **42:** 1053 (Dec.) 1939.

2. Robinson, L. J., and Osgood, Robert: Comparative Effects of Phenobarbital and Dilantin Sodium in the Treatment of Epilepsy, J. A. M. A. **114:** 1334-1336 (April 6) 1940.

limits throughout. The blood pressure was 118 systolic, 82 diastolic. The carotid sinus pressure was normal.

Laboratory examinations showed the following: Urinalysis (four specimens): The urine was amber and acid; specific gravity was from 1.020 to 1.023; it showed a faint trace of albumin and no sugar; examination of the sediment was negative.

Hematology: The hemoglobin was 94 per cent (Sahli), red blood cell count 4,880,000, color index 0.9, white blood cells 8,000, differential count: polymorphonuclear leukocytes 74 per cent, lymphocytes 21 per cent, eosinophils 4 per cent and transitionals 1 per cent. The red cells appeared normal.

Blood Chemistry: Nonprotein nitrogen was 28 mg. per hundred cubic centimeters of blood and uric acid 4 mg.; blood sugar tolerance, fasting 100 mg., one-half hour 120 mg., one hour 100 mg., two hours 100 mg., three hours 90 mg. and six hours 110 mg. per hundred cubic centimeters of blood.

The basal metabolic rate was minus 16 per cent. The Hinton test of the blood gave negative results.

Lumbar Puncture: The initial pressure was 85 mm. of water and the dynamics were normal; 10 cc. of clear colorless fluid was removed and the final pressure was 70 mm.; there were no cells, the total protein was 50 mg. per hundred cubic centimeters of fluid; globulin test negative, and sugar 66 mg.; Wassermann and Hinton tests gave negative results; the colloidal gold curve was 1122222210.

Roentgenogram of skull: Lateral and anteroposterior stereoscopic views showed no abnormality.

The pneumo-encephalogram revealed a normal ventricular system. There were small pools of air in the frontal and temporal areas more noticeably on the left side.

The electro-encephalogram was abnormal, showing during rest waves with a frequency of from 6 to 10 bilaterally, and during hyperventilation additional waves with a frequency of from 3 to 5 from the left hemisphere.

Since the patient continued to have seizures despite the phenobarbital medication, he was advised to take dilantin sodium 1½ grains (0.1 Gm.) morning and night, in addition to phenobarbital 1½ grains nightly. From time to time both he and his mother reported with favorable comments on his incidence of seizures.

On April 15, 1940, eleven months after his first visit to the outpatient clinic, the patient returned with the statement that he had lost two successive positions because of recurrent seizures. He became disheartened and reported that on April 4, 1940, he had ingested forty-five capsules (4.5 Gm. [67½ grains]) of dilantin sodium. These were taken at 4:45 p. m. At 5:15 he felt extremely drowsy and dizzy and trembled a little. At 5:20 he became unconscious. His mother called the local hospital, which sent its ambulance physician. The latter found the patient in deep coma. The skin was cold and clammy. The pupils reacted to light and in accommodation. The jaws were firmly closed. All the reflexes were reported normal. The pulse was regular, with a rate of 74. Cardiac, pulmonary and abdominal examinations revealed no unusual conditions. All efforts to arouse the patient were futile. Nikethamide 1.5 cc. (25 per cent aqueous solution of pyridine-beta-carboxylic acid diethylamide) subcutaneously produced no effect.

The patient was hospitalized in his home community. Nikethamide 3 cc. was administered intravenously. By this time attempts at gastric lavage evoked struggling on the part of the patient. He vomited small amounts of yellowish mucus. He was given strychnine sulfate (0.001 Gm. [one-sixtieth grain]) and caffeine sodiobenzoate (0.5 Gm. [7½ grains]). The patient began to move restlessly and continued his aimless movements for one hour and twenty minutes, at the end of which time he regained complete consciousness and was fully oriented. Emesis was induced and the patient vomited 12 ounces (360 cc.) of brownish fluid. The only residual effects noted were severe headache and a strong desire to urinate, accompanied by a sensation of continuous urethral drip. The latter cleared in three or four days, during which time tincture of hyoscyamus 10 minims (0.65 cc.) three times a day was administered.

On the fourth hospital day the patient had an epileptic seizure. On the seventh day he was discharged ambulatory and recovered. He was advised to take dilantin sodium 0.1 Gm. (1½ grains) three times a day. When seen six weeks later he showed no unusual sequelae.

STUDIES IN BLOOD PRESERVATION:
THE SHAPE OF THE CONTAINER

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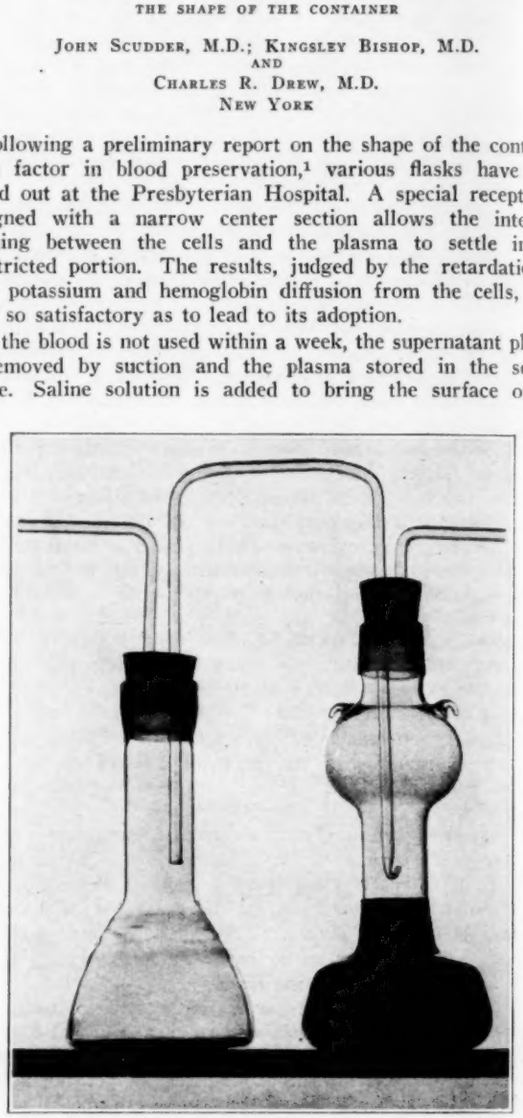
AND
CHARLES R. DREW, M.D.
NEW YORK

Following a preliminary report on the shape of the container as a factor in blood preservation,[1] various flasks have been tested out at the Presbyterian Hospital. A special receptacle[2] designed with a narrow center section allows the interface forming between the cells and the plasma to settle in the constricted portion. The results, judged by the retardation of both potassium and hemoglobin diffusion from the cells, have been so satisfactory as to lead to its adoption.

If the blood is not used within a week, the supernatant plasma is removed by suction and the plasma stored in the second bottle. Saline solution is added to bring the surface of the



Flasks for blood preservation. The container on the right shows the formation of the interface between plasma and cells in the narrow section of the bottle. The supernatant plasma is transferred into the container on the left by suction.

plasma up into the neck of the flask. This accomplishes a dual purpose. The addition of the saline solution tends to keep the fibrin in solution, and the reduction of the interface retards surface denaturation.

The stability of both blood and plasma is further enhanced by drawing the sample into an atmosphere of carbon dioxide, thereby retarding the formation of ammonia as well as increasing the hydrogen ion concentration.[3] This procedure is readily accomplished by flushing out the flask with carbon dioxide and then introducing the blood into the bottom of the container.

These simple factors recommend themselves, as they retard the deterioration of preserved blood.

630 West One Hundred and Sixty-Eighth Street.

This study was conducted under a grant from the Blood Transfusion Betterment Association of New York.

From the Surgical Pathology Laboratory of Columbia University College of Physicians and Surgeons.

1. Scudder, John; Drew, C. R.; Corcoran, Dorothy R., and Bull, D. C.: Studies in Blood Preservation, J. A. M. A. **112**: 2263-2271 (June 3) 1939.

2. Scudder, John: Shock; Blood Studies as a Guide to Therapy, Philadelphia, J. B. Lippincott Company, 1940.

3. Smith, Margaret E.; Tuthill, Elizabeth; Drew, C. R., and Scudder, John: Studies in Blood Preservation: Some Effects of Carbon Dioxide, J. Biol. Chem. **133**: 499 (April) 1940.

WESTERN EQUINE ENCEPHALOMYELITIS FOLLOWING ACCIDENTAL INOCULATION WITH CHICK EMBRYO VIRUS

REPORT OF A FATAL HUMAN CASE WITH NECROPSY

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A number of cases of equine encephalomyelitis have been recorded as occurring in man. In none of these, however, has the incubation period been established.[1] In 1939 Fothergill, Holden and Wyckoff[2] reported a case in which equine encephalomyelitis occurred in a woman aged 30 ten days after she was employed in a laboratory, where she worked with chick embryo virus. The route of her infection could not be ascertained although there were rumors of possible injury to a finger from a gold pointed needle breaking off in it. Careful investigation failed to establish the truth of this rumor. No report was made by the patient, although strict orders for reporting the slightest accident were constantly enforced and observed and no damaged needle was turned in.

Since I could not find a single instance in the literature in which the incubation period in the human being was known, the case reported here seemed worth recording.

REPORT OF CASE

On June 16, 1939, about 4:30 p. m., Dr. S., aged 57, a prominent veterinarian, was centrifuging some highly concentrated living chick embryo virus of western equine encephalomyelitis in the vaccine room of his large commercial laboratory. The virus had been placed in the centrifuge and Dr. S. was operating the rheostat. It was the first time the new machine had ever been used. Apparently too much power was applied and the virus was thrown out of the top and all over the lid of the centrifuge. The force was so great that virus was spattered all over the walls and sprayed the windows so that the virus ran in fine rivulets down the window panes. Dr. S. had on no mask or goggles, and even his glasses were covered with the virus. A technician standing near him who was supplied with mask and goggles was also sprayed from head to foot to such an extent that she was forced to wipe both her goggles and her shoes with mercury bichloride solution. Later another screen was placed in the machine and Dr. S. again operated it without mishap. Prior to this date and thereafter Dr. S. was not in the vaccine room and no record of any further contact with virus up to the time of his death could be elicited. On June 30, fourteen days after the accident, he had a very severe headache, which was accompanied by nausea and vomiting. On July 1 his temperature was 103 F. and the nausea, vomiting and headache persisted. His general condition grew progressively worse. Spasticity and athetosis of the upper extremities developed. There was also some spasticity of the lower extremities. He became quite irritable, then delirious and finally somnolent.

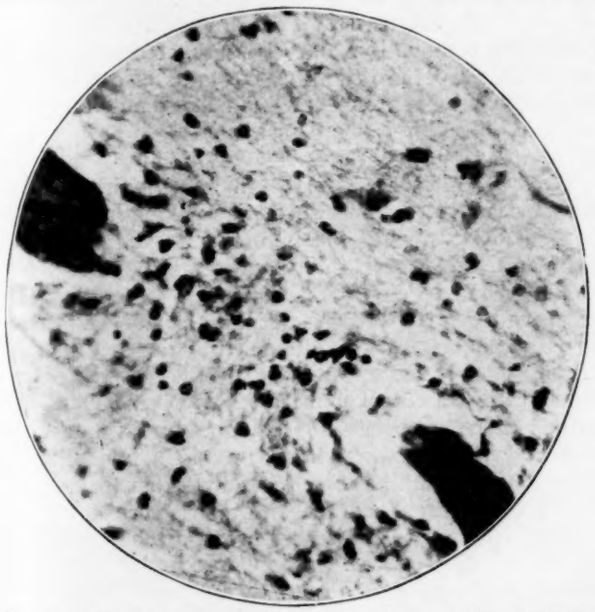


Fig. 1.—Section of minute inflammatory lesion, involving borders of perivascular spaces, under high power.

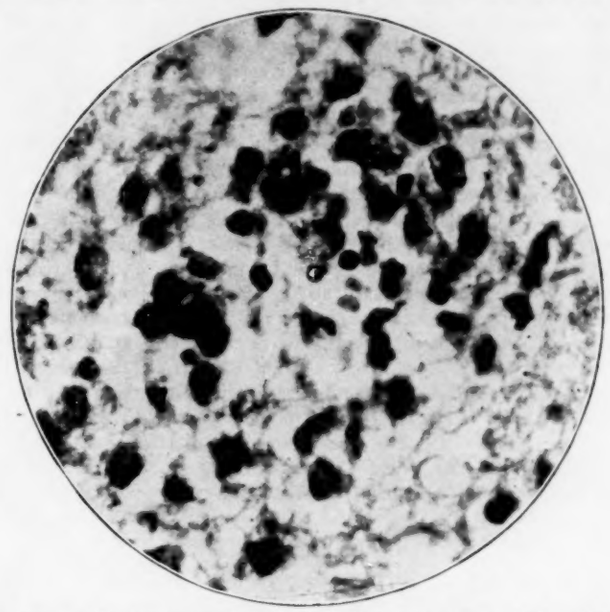


Fig. 2.—Oil immersion view of small focal lesion in the brain. Note preponderance of polymorphonuclear leukocytes and breaking up of ground substance.

On physical examination following admission to the hospital the patient, a moderately corpulent man, was obviously quite sick. No eye signs were present but there was spasticity of the extremities, which was most marked in the arms; and athetoid movements of the hands were quite striking.

On admission his temperature was 103.8 F., his pulse rate 84 per minute. Following admission his temperature ranged from 103 to 105 F. He was given anti-equine encephalomyelitis serum. A severe reaction followed the intravenous administration of the first 200 cc. of the serum, the temperature rose to 107 F. and the pulse rate rose to 140 per minute, shortly followed by a drop of both pulse and temperature to almost normal. Because of his high degree of sensitivity, it was thought, therefore, to employ guinea pig serum, which was tried without reaction. He did not rally, however, and died at 7:30 a. m. July 7, eight days after taking sick.

Laboratory examinations showed a white count ranging from 11,300 to 19,400; the spinal fluid showed 97 white blood cells, of which 92 per cent were lymphocytes and 8 per cent were polymorphonuclear leukocytes; there were 11 red blood cells and the globulin test was positive. The total protein of the spinal fluid was 40 mg. per hundred cubic centimeters one day after entry and the count mounted to 175 white and 134 red blood cells. The color changes shown in the gold curve were 0000110000.

Necropsy.—This was performed forty-five minutes after death. Aside from a terminal left lobar pneumonia, moderate cardiac hypertrophy, a nodular colloid goiter and medullary softening of the adrenals, the chief pathologic changes of interest were confined to the brain. The subarachnoid space contained considerable increase in fluid and the cut surface of the brain appeared unusually moist. The brain weighed 1,620 Gm. On section through the cortex many pinpoint petechiae were seen. The same petechiae were observed in the region of the basal nuclei. Otherwise the brain and spinal cord were not noteworthy.

From the Department of Pathology, St. Luke's Hospital.

1. Olitsky, Peter K: Infection with Equine Encephalomyelitis Virus, in Brennemann, Joseph: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, 1939, vol. 14, chapter VII, p. 35. Farber, Sidney; Hill, Allen; Connerly, Marion L., and Dingle, J. H.: Encephalitis in Infants and Children, J. A. M. A. **114:** 1725 (May 4) 1940.

2. Fothergill, L. D.; Holden, Margaret, and Wyckoff, R. W. G.: Western Equine Encephalomyelitis in a Laboratory Worker, J. A. M. A. **113:** 206 (July 15) 1939.

Microscopic Examination: Hematoxylin and eosin, Masson's trichrome, Bielschowsky, Pal-Weigert, Nissl and scarlet red stains were employed on sections from the brain.

The most uniform lesion encountered was the presence of numerous pinpoint accumulations of polymorphonuclear leukocytes admixed with a few monocytes and lymphocytes. In these minute foci there was marked breaking up and fragmentation of the ground substance. Often these tiny infiltrates could be seen abutting directly on the borders of tiny blood vessels. Not infrequently they seemed to arise from these little vessels and involve the wall of such vessels (fig. 1). Practically every section taken from different areas in the brain showed from one to several of these miniature infiltrates, which were usually of such a size that they could often be incorporated in the high power field of the microscope (fig. 2). The next most frequent lesion consisted of pinpoint interstitial hemorrhages of about the same size as the infiltrations, being apparently unrelated to any blood vessel unless it should be a tiny capillary the walls of which had become destroyed. Perivascular hemorrhages and infiltrations of polymorphonuclear leukocytes, monocytes and lymphocytes also were encountered in many sections. Advanced degenerative changes in ganglion cells were also found. The arterioles and capillaries often showed endothelial swelling, and sometimes hyaline thrombi were seen. There was a moderate degree of interstitial edema. At the base and in the medulla the damage was most marked. In some areas of the cortex the pia-arachnoid showed a mild infiltration with polymorphonuclear leukocytes and monocytes. This arachnoid infiltration did not show in many areas. The spinal cord showed only a mild leukocytic infiltration of the pia.

COMMENT

The incubation period following intranasal inoculation with western encephalitis virus in monkeys as carried out by Wyckoff and Tesar [3] showed that the temperature peak occurred around the fifth or sixth day following inoculation. This is later than that reached in the eastern disease and the febrile stage in their experiments lasted longer with western infection, although the temperature did not rise as high or fall as precipitately as with eastern virus disease. Moreover, the stage of paralysis developed more slowly in western infection and the comatose stage preceding death was of greater duration than in the eastern disease. These workers were unable to produce the disease by way of the gastrointestinal tract by means of a stomach tube. Dr. Beatrice Howitt [4] of the University of California has likewise been unable to infect guinea pigs by stomach tube provided no virus is regurgitated back into the mouth. In the horse the incubation period is said to range from one to three weeks.

Our patient was sprayed liberally with the virus on June 16 at 4:30 p. m. and his first symptoms became manifest on June 30, fourteen days after the accident. He died on July 7, eight days after the onset of fever, nausea and vomiting. The gross and microscopic appearances in the brain were more or less typical of equine encephalomyelitis and correspond with the changes observed by other workers. Unfortunately the brain was removed, packed in solid carbon dioxide and sent to Washington, where it was not examined for some time after arrival there. In a communication from the Public Health Service it was stated that the brain was contaminated and that no refrigeration was present on arrival of the material; hence it is not strange that it was impossible to identify or isolate any virus from the brain, since it vanishes very quickly after death.

CONCLUSIONS

A laboratory worker was accidentally inoculated by a spray of highly virulent chick embryo virus of western encephalitis. The incubation period was fourteen days from the time of accidental experimental inoculation to the onset of symptoms. The probable port of entry was through the upper respiratory tract, since the virus was spattered over his face. Careful check failed to reveal any contact with virus for some weeks prior or subsequent to this accidental inoculation.

3. Wyckoff, Ralph W. G., and Tesar, Walter C.: Equine Encephalomyelitis in Monkeys, J. Immunol. **37**: 329 (Oct.) 1939.
4. Howitt, Beatrice: Personal communication to the author.

Special Clinical Article

SOME RECENT ADVANCES IN VITAMIN THERAPY

CLINICAL LECTURE AT NEW YORK SESSION

T. D. SPIES, M.D.
CINCINNATI
D. P. HIGHTOWER, M.D.
AND
L. H. HUBBARD, M.D.
BIRMINGHAM, ALA.

Long after beriberi, rickets, scurvy and pellagra were recognized and described by physicians, the concept of nutritional deficiency diseases arose. With the development of this concept, a new chapter in medicine came into being. Of late considerable research has been directed toward the isolation and synthesis of so-called accessory food factors, more commonly known as vitamins, and some of these substances have been found effective in the treatment of beriberi, rickets, scurvy and pellagra. The years following the brilliant investigations which led to the isolation, synthesis and clinical trial of thiamine hydrochloride, nicotinic acid, riboflavin, vitamin E, vitamin B_6 and pantothenic acid have, however, been marked by a period of confusion. The literature with regard to these vitamins, and to the deficiencies arising from a suboptimal amount of them, is vast and often contradictory. The problem is so complex and the precise knowledge so meager that we must accept the point of view that a rising curve of complexity is on us. The accompanying illustration shows this complexity. Accordingly, it seems wise to restrict this report to the present status of a few of the therapeutic advances made in the field of nutrition since 1936.

1936: THIAMINE HYDROCHLORIDE

The synthesis of vitamin B_1 (thiamine hydrochloride) in 1936 accelerated clinical investigation and made possible intensive study of the nature and symptomatology of beriberi. Beriberi, in its severe form, affects predominantly the peripheral nervous and the cardiovascular systems. It is characterized by a symmetrical peripheral neuropathy accompanied by degeneration and atrophy of the muscles supplied by the affected nerves, and by cardiovascular disturbances which include edema, cardiac dilatation, speeded circulation, high venous pressure and prolonged electrical systole. The study of many patients with beriberi has shown that they experience a long period of ill health, characterized by prodromal symptoms, before the recognizable symptoms of the disease appear. These prodromal symptoms include loss of weight, strength and appetite, periodic vertigo, burning sensations in various parts of the body,

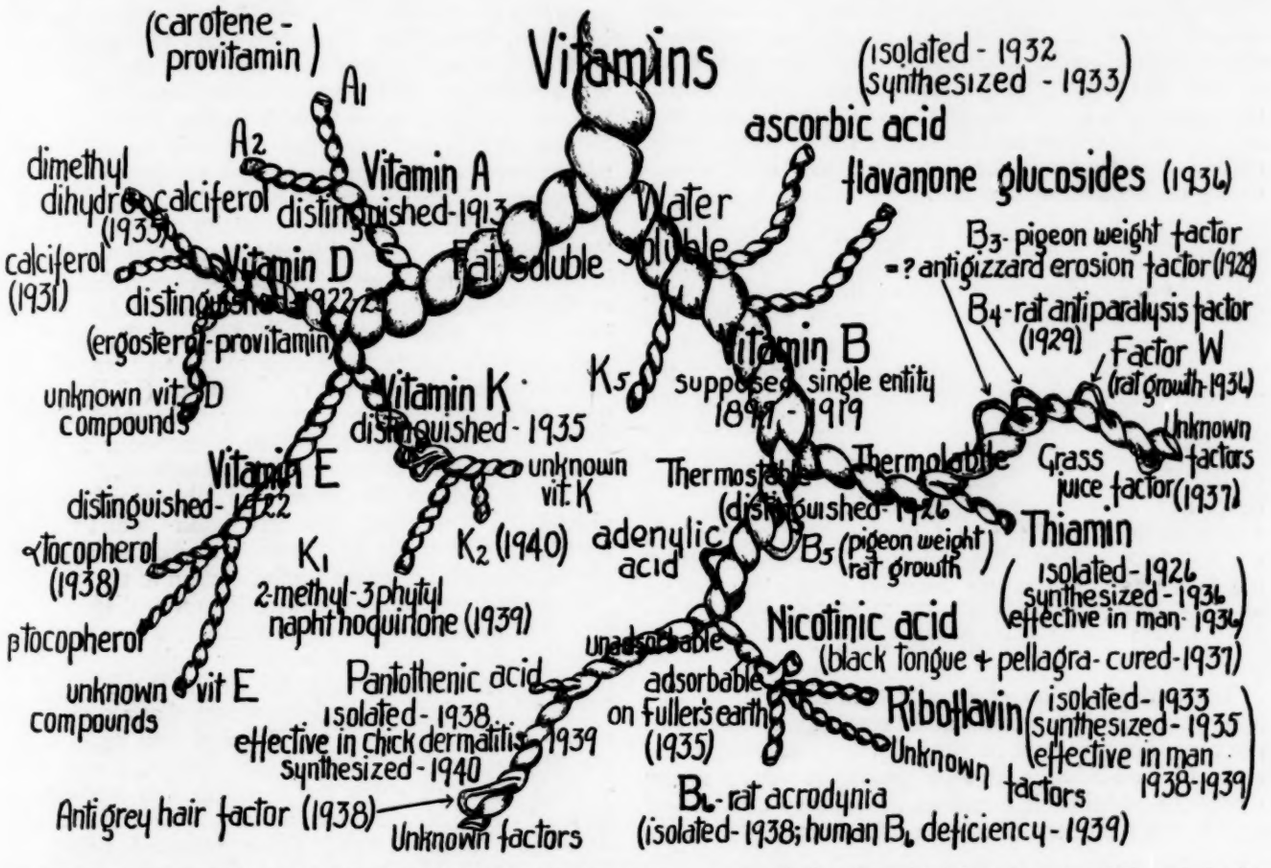
Owing to lack of space, this article is abbreviated here by the omission of a bibliography which will appear in the reprints.

Read in the Medical Division of the General Scientific Meetings at the Ninety-First Annual Session of the American Medical Association, New York, June 11, 1940.

The present paper includes a brief review of the work done by many investigators. The studies conducted by the authors during the past four years have been under the auspices of the Department of Internal Medicine of the University of Cincinnati College of Medicine until the past year, at which time a cooperative project between the Department of Preventive Medicine of the University of Texas Faculty of Medicine and the Department of Internal Medicine of the University of Cincinnati College of Medicine was initiated. The heavy expenses of these studies were borne in large part by the John and Mary R. Markle Foundation, the Rockefeller Foundation, the David May Fund, Anheuser-Busch, Inc., Eli Lilly & Co., Mead Johnson & Co. and E. R. Squibb & Sons.

nervousness, numbness, loss of sensation in the extremities, and cramps and tenderness of the muscles.

Vitamin B_1 is of considerable value in the treatment of beriberi and of the acute neuropathy associated with chronic alcoholic addiction, pellagra and pregnancy. Enough information is available to warrant the trial, under controlled conditions, of this substance for persons who have peripheral neuritis associated with dietary deficiency. Vitamin B_1 does not act as an analgesic, and it is our belief that this substance is most useful in the amelioration of the early disorders caused by a deficiency of vitamin B_1. The administration of synthetic vitamin B_1 (thiamine hydrochloride) to persons with acute beriberi relieves the cardiovascular disturbances, induces improvement in response of the muscles innervated by affected peripheral and cranial nerves, restores the normal electrical conductivity of peripheral nerves, relieves gastrointestinal dysfunction resulting from thiamine deficiency, increases carbohydrate tolerance and decreases bisulfite binding substances in the blood. In cases of subclinical thiamine deficiency it often increases the appetite, strength and feeling of well-being and relieves the symptoms arising from early neurologic lesions of beriberi.



Diagrammatic representation of the interrelationship of the vitamins. They are schematically differentiated into the water-soluble and the fat-soluble fractions; the latter group is further separated into its thermolabile and its thermostable components. Certain of these substances have been shown to be essential to human nutrition and effective in the treatment of specific deficiency diseases. The physiologic properties of many are as yet undetermined.

1937-1938: NICOTINIC ACID

The isolation of nicotinic acid amide from liver concentrates marks a milestone in our progress in the study of pellagra. Nicotinic acid amide, nicotinic acid, sodium nicotinate, the diethyl amide of nicotinic acid (nikethamide) and other related compounds have been found to relieve many of the symptoms of pellagra. Clinical pellagra is a systemic disease which affects chiefly the alimentary tract, skin and nervous system. Typical glossitis, which is characterized by swelling and reddening of the margins and tip of the tongue and which, as the disease progresses, extends to involve the entire tongue, is one of the earliest symptoms diagnostic of the disease. Stomatitis, gingivitis and pharyngitis also develop and progress in a similar way. These lesions of the mucous membranes are often infected with Vincent's organisms. Nausea, vomiting, ptyalism, diarrhea and abdominal distention are usually advanced symptoms of the disease. The dermal lesions of pellagra may occur on any part of the body. These lesions usually are bilaterally symmetrical and are sharply demarcated from the adjacent healthy skin. At first the erythematous area somewhat resembles sunburn, but later in the course of the disease the color changes to reddish brown, desquamation begins and the underlying skin is seen to be abnormally red and thickened. Permanent pigmentation may develop following frequent recurrences of the dermatitis. In pellagrins, severe mental disturbances, such as apprehension, confusion, disorientation, hallucinations, mania and delirium, are an indication of a very advanced stage of the disease. However, these advanced symptoms are preceded by a period during which the patient complains of loss of weight and strength, lassitude, abdominal pain, numbness, nervousness and forgetfulness. An initial nervous syndrome, characterized by hyperesthesia to all forms of sensation, increased psychomotor drive, anxiety and apprehension with a tendency toward depression, weariness and increased fatigability, headaches and sleeplessness, is typical of this prodromal period. Recognition

of these early symptoms and immediate application of therapy prevents the development of classic pellagra.

The administration of adequate amounts of nicotinic acid, or compounds acting similarly, to persons with acute or relapsed pellagra will cause fading of the fiery red lesions of the mucous membranes and striking improvement in the Vincent's infection associated with it, revive the appetite and restore normal alimentary function, sometimes with a return of gastric hydrochloric acid, increase strength and feeling of well-being, and restore to normal deranged mental functions, provided they result from pellagra and are not of too great chronicity. In cases of subclinical pellagra these synthetic chemical substances will relieve indigestion, diarrhea, burning of the tongue and stomach, burning and itching of the skin, dizziness, forgetfulness, confusion, insomnia and the symptoms of the initial nervous syndrome. Nicotinic acid will also cause disappearance of the abnormal ether-soluble red pigments which are present in the urine of pellagrins, increase the content of coenzymes I and II in the blood and urine and increase the nicotinic acid content of the blood and urine of both normal persons and persons who have a deficiency of nicotinic acid amide.

1938-1939: RIBOFLAVIN

We shall say little about riboflavin deficiency, as Dr. Sebrell has presented most of the essential points. The importance of riboflavin in human nutrition was observed independently by Sebrell and Butler [1] and by the Vilters and Spies.[2] Lesions at the corners of the mouth (cheilosis) were first described by Sebrell and Butler as a typical manifestation of riboflavin deficiency. Erosions around the eyes and a shark skin appearance of the skin over the nose are also characteristic of a deficiency of this substance. Itching, burning and excessive dryness of the eyes, photophobia, granulation and extreme redness of the conjunctiva, particularly of the lower lids, are rather common complaints among persons suffering from riboflavin deficiency. These conjunctival manifestations are often associated with keratitis.

The administration of riboflavin is followed by disappearance of the cheilosis and "shark skin" lesions of the nose, improvement in general vigor, increase in the sense of well-being, and relief from the ocular symptoms. In addition, it increases the efficacy of nicotinic acid in the treatment of certain pellagrins.

1939-1940: VITAMIN K AND VITAMIN B_6

Vitamin K.—Vitamin K, a fat-soluble vitamin, is essential for the maintenance of a normal concentration of prothrombin in the blood. Animal experimentation and clinical studies have shown that certain hemorrhagic tendencies are due to a low plasma prothrombin resulting from a vitamin K deficiency. Absorption of this fat-soluble vitamin is dependent on the presence of bile in the intestine rather than on the adequacy of vitamin K in the diet. Lowered prothrombin concentration may occur in conditions in which extensive intestinal lesions interfere with absorption or, more frequently, in conditions in which bile is excluded from the intestine by obstruction of the common bile duct. In such cases the administration of vitamin K will restore the normal prothrombin level. Bile salts, of course, must be given along with the orally administered vitamin in cases in which bile is not present in the intestine; otherwise the vitamin will not be absorbed. Recent work also indicates that newborn infants have a vitamin K deficiency in the first few days of life and that the administration of vitamin K will prevent and cure the hemorrhagic diathesis in at least many cases of "hemorrhagic disease of the newborn."

Pyridoxin (vitamin B_6).—Clinical studies to determine whether vitamin B_6 is essential to human nutrition were undertaken in 1938, soon after the artificial synthesis of this vitamin was accomplished. Spies, Bean and Ashe,[3] in a preliminary report, described the favorable symptomatic response to vitamin B_6 by four persons who failed to recover completely when on a selected diet supplemented with thiamine hydrochloride, riboflavin and nicotinic acid. The symptoms responding favorably to vitamin B_6 included extreme nervousness, insomnia, irritability, cramping pains in the stomach, weakness, muscular rigidity, and difficulty and awkwardness in walking. More recently we have treated twenty additional patients with similar results. Vilter, Schiro and Spies [4] reported that this vitamin, when administered in large amounts, produced a slight reticulocytosis in persons who have macrocytic anemia associated with pellagra or pernicious anemia in relapse. These studies, however, do not imply that vitamin B_6 is an anti-pernicious anemia factor or the extrinsic factor of Castle. Improvement has been noted following the intravenous administration of vitamin B_6 to some patients with idiopathic epilepsy and to persons with amyotrophic lateral sclerosis. One of us (T. D. S.) has seen three cases of myasthenia gravis which showed pronounced improvement within twenty-four to forty-eight hours after the injection of vitamin B_6.

On the basis of the dramatic and beneficial effect of vitamin B_6 in relieving muscular weakness and rigidity, an effort was made to determine whether a similar response would follow its administration to persons with Parkinson's syndrome, a severe lingering disease characterized by tremor of the extremities, weakness, delay of voluntary motion and muscular rigidity. In April of this year Dr. Norman Jolliffe of the New York University College of Medicine reported at a symposium on vitamins at Mount Sinai Hospital, and again before the Minnesota State Medical Association, the effect of vitamin B_6 in relieving the rigidities and weakness in certain cases of paralysis agitans (Parkinson's syndrome). More recently Spies reported before the Illinois State Medical Society the results of studies concerning the use of vitamin B_6 in eleven selected cases of parkinsonism of at least four years' duration, eight of which were arteriosclerotic and three postencephalitic. Within a few minutes there was much improvement in the latter three. Rigidity was decreased significantly and the patients were able to walk without the usual stiffness. Two of the arteriosclerotic patients showed definite improvement, five were unchanged and one was considerably worse. Dr. Jolliffe [5] has stated that in a study of thirty patients with paralysis agitans he observed "no apparent improvement in the postencephalitic group, little or no improvement in any group of patients hospitalized for over three years and dramatic improvement in approximately 20 per cent of the patients with nonpostencephalitic parkinsonism who had

1. Sebrell, W. H., and Butler, R. E.: Riboflavin Deficiency in Man: A Preliminary Note, Pub. Health Rep. **53**: 2282 (Dec. 30) 1938.
2. Vilter, R. W.; Vilter, Sue P., and Spies, T. D.: Relationship Between Nicotinic Acid and a Codehydrogenase (Cozymase) in Blood of Pellagrins and Normal Persons, J. A. M. A. **112**: 420 (Feb. 4) 1939.
3. Spies, T. D.; Bean, W. B., and Ashe, W. F.: A Note on the Use of Vitamin B_6 in Human Nutrition, J. A. M. A. **112**: 2414 (June 10) 1939.
4. Vilter, R. W.; Schiro, H. S., and Spies, T. D.: Effect of Synthetic Vitamin B_6 on the Hemopoietic System of Human Beings, Nature **145**: 388 (March 9) 1940.
5. Jolliffe, Norman: Personal communication to the authors.

been helpless for less than one year." These preliminary observations indicate to the authors that rigidity in some cases seems to be decreased and that vitamin B_6 should have more careful study. It seems likely that some persons with Parkinson's syndrome may have an associated vitamin B_6 deficiency, for indeed it is the close resemblance of the rigidity and awkwardness in walking observed in patients suffering from either disease which prompted us to administer vitamin B_6 to those with Parkinson's syndrome.

Many more studies are necessary before conclusive statements can be made concerning the effect of this vitamin on persons with various diseases. It must be emphasized that a sedative effect of vitamin B_6 may be responsible, in part at least, for the rapidity with which symptoms are relieved and that the administration of this vitamin is warranted only under controlled conditions.

1940: VITAMIN E, YEAST ADENYLIC ACID AND PANTOTHENIC ACID

Vitamin E.—For several years it was believed that vitamin E was concerned specifically with reproduction. During the past decade, however, a definite relationship between an inadequate intake of vitamin E and the normality of the cross striated musculature of the body has been established. Characteristic muscular atrophy occurs in widely divergent animal species when vitamin E is withdrawn from their diets. Restoration occurs following the intramuscular injection of synthetic alpha-tocopherol (vitamin E). During the past year Wechsler [6] and Spies and Vilter [7] observed independently that synthetic alpha-tocopherol has a beneficial effect on occasional persons with amyotrophic lateral sclerosis. The injection of 500 mg. of alpha-tocopherol in sterile oil is effective, at least temporarily, in relieving neuromuscular symptoms, roaring sensations in the ears, anorexia, and insomnia of selected persons with malnutrition but without clinical evidence of pellagra, beriberi or riboflavin deficiency. We have observed striking improvement in a few of these people following the administration of vitamin E, but it is difficult to measure objectively the degree of improvement. It would seem that the patients who experience the greatest relief are those who also have some deficiency of vitamin E.

Clinical studies of the therapeutic effect of vitamin E are still somewhat in an experimental stage, and until further work is done the administration of this substance is warranted only under controlled conditions.

Yeast Adenylic Acid.—Adenylic acid is a constituent of the pyridine dinucleotides, coenzymes I and II, and since these intracellular enzymes are fundamental to physiologic processes it was felt that adenylic acid merited consideration for study in the treatment of persons with mixed deficiency diseases. Accordingly, we administered yeast adenylic acid to normal persons and to poorly nourished persons who had symptoms which were not relieved by nicotinic acid, thiamine hydrochloride, riboflavin, vitamin B_6 or vitamin A. The injection of from 3 to 20 mg., dissolved in sterile physiologic solution of sodium chloride, within fifteen seconds produced involuntary, deep, gasping inspiration, fluttering sensation in the upper part of the abdomen and a feeling of fulness in the head. All patients had transient flushing of the neck and face, and the pupils became widely dilated. These symptoms vanished within a few minutes and left no evidence of a harmful effect. Less intense symptoms of the same type followed the administration of a single dose of 200 mg. of adenylic acid by mouth. Six patients with malnutrition who had intense burning of the oral mucous membranes but no diagnostic evidence of pellagra were relieved following treatment with adenylic acid. The administration of this substance together with nicotinic acid to a series of pellagrins in relapse seemed to increase the effectiveness of the nicotinic acid. However, because of the severe reactions produced by the intravenous injection of yeast adenylic acid we do not recommend its administration to human beings.

Pantothenic Acid.—The structure of pantothenic acid (the chick antidermatitis factor) has been determined and early in 1940 its synthesis was accomplished. Now that it is becoming available for clinical investigation, studies on its relation to the blood, urine and tissues of human beings are in progress. Since there was no information regarding the possible toxicity of pantothenic acid, we administered this substance, under controlled conditions, to a series of normal persons and found that at least 100 mg. may be injected intravenously without producing a reaction or causing a significant change in the blood pressure, pulse or respiration. Spies, Stanbery, Williams and Jukes [8] observed that the pantothenic acid content of the blood is increased soon after injection but returns to its previous level within twenty-four hours. Stanbery, Snell and Spies [9] have shown that the pantothenic acid content of the blood of persons having severe deficiency diseases, such as pellagra, beriberi and riboflavin deficiency, is from 23 to 50 per cent lower than in normal persons and that with a rise in the pantothenic acid content there is a simultaneous increase in the riboflavin content of the blood. The patients with an abnormally low concentration of pantothenic acid in the blood have also had less than normal in the urine. These observations suggest that pantothenic acid is important in human nutrition.

GENERAL CLINICAL CONSIDERATIONS OF DEFICIENCY DISEASES

Factors Operating to Produce Deficiency States.—The factors that operate to produce nutritional deficiency diseases are an inadequate intake, increased need, diminished absorption or utilization, or increased destruction or excretion of the essential nutritional substance or substances. Clinical study of deficiency disease syndromes in 3,500 persons, including the 1,500 reported in this paper, has shown that single deficiency states seldom exist. This is not surprising since the dietaries of persons in whom these diseases most frequently occur are deficient in many essential nutrients. The resultant clinical picture is extremely complex; we frequently see evidence of pellagra, beriberi, riboflavin deficiency, scurvy, vitamin B_6 deficiency, vitamin A deficiency and anemia in the same person. The diagnosis of one clinical deficiency syndrome, therefore, necessitates a thorough search for others.

Factors of Safety Operating to Correct Deficiency States.—Certain factors of safety operate to protect the body and to compensate for a deficiency of these essential substances once the deficiency has set in. A wide margin of safety exists between the beginning of a dietary deficiency disease and death from it. We have reported cases in which rest alone was followed by some

6. Wechsler, I. S.: Recovery in Amyotrophic Lateral Sclerosis Treated with Tocopherols (Vitamin E): Preliminary Report, J. A. M. A. **114**: 948 (March 16) 1940.

7. Spies, T. D., and Vilter, R. W.: A Note on the Effect of Alpha-Tocopherol (Vitamin E) in Human Nutrition, South. M. J. **33**: 663 (June) 1940.

8. Spies, T. D.; Stanbery, S. R.; Williams, R. J., and Jukes, T. H.: Unpublished observations.

9. Stanbery, S. R.; Snell, E. E., and Spies, T. D.: Unpublished observations.

improvement and, in certain instances, by healing of the lesions characteristic of a specific deficiency state. More recently we have observed a significant increase in the blood concentration of coenzymes I and II following rest in bed. When treating persons with nutritional diseases, one should therefore curtail their activities as much as possible until restoration of the affected tissue to normal is under way. Another factor of safety is the storage of these essential substances which takes place to some extent in the tissues. Also the body tends to excrete less when a deficiency exists. Nevertheless there is a limit to this self regulation and, if the deprivation of these substances continues, irreparable damage to the tissues will result.

PRINCIPLES OF THERAPY FOR DEFICIENCY DISEASES

General Therapy.—The following general principles of therapy are applicable to all deficiency diseases: Each patient must be considered as an individual problem and treatment prescribed accordingly. A well balanced diet of 4,500 calories, rich in protein, minerals and vitamins, should be eaten each day. The type of food, the mode of administration and the time and frequency of feeding in the more severe cases are dependent on the patient's condition and on his ability to tolerate food. Complete reliance on dietary therapy, however, is not recommended, for the necessary protective substances are present in too small amounts to be effective in cases of well developed deficiency diseases. Furthermore, persons of the lower income group who are most frequently affected by nutritional diseases cannot afford to buy the relatively expensive foods rich in vitamins and protein. Specific therapeutic agents, then, should be given as supplements to a well balanced diet. In the very severe case hospitalization is advisable, for the combined services of a physician, nurse and dietitian are essential. The patient should be kept at complete rest in bed until convalescence is well established. If for any reason the food requirement is increased, efforts must be made to eliminate the cause. Appropriate symptomatic therapy and treatment of coexistent diseases are of course desirable. Treatment in all cases should be based on all the clinical evidence available.

Specific Therapy.—Specific therapy in the form of large doses of synthetic chemical substances induces more rapid and dramatic remission of symptoms of the specific deficiency diseases, shortens convalescence in the severe case, and assures more certain recovery. The indication for therapeutic use of synthetic vitamins and concentrates of yeast and liver is very large indeed, but indiscriminate use is not consistent with the interests of the patient.

Beriberi is treated best by giving pure crystalline vitamin B_1 (thiamine hydrochloride). The administration of 20 mg. a day in 10 mg. doses is recommended for the average case of beriberi in the adult, and for the severe case from 50 to 100 mg. administered in divided doses. Ten mg. daily may be sufficient for the mild case. Infantile beriberi is treated best by giving 5 mg. of thiamine hydrochloride, dissolved in sterile physiologic solution of sodium chloride, twice a day, or 10 mg. by mouth each day. The treatment of the nursing child will be greatly aided by giving the mother satisfactory antiberiberic treatment. Vitamin B_1 may be administered either orally or parenterally, but the latter method is preferred in the acute case because of the greater ease in giving massive doses, the greater certainty of absorption and the more rapid improvement which follows.

Nicotinic acid, nicotinic acid amide and sodium nicotinate are effective in the treatment of pellagra. These substances may be administered orally in tablets or capsules, or parenterally, dissolved in sterile physiologic solution of sodium chloride. The average adult patient will respond to the oral administration of 500 mg. daily, given in divided doses of 50 mg. each, though as much as 1,000 mg. a day may be required in the very severe cases. The parenteral dose varies from 50 to 80 mg. daily, injected intravenously in doses of from 10 to 15 mg. Nicotinic acid amide has an advantage as a therapetuic agent in that it does not produce vasodilatation of the skin or an increase in the temperature of the skin which so frequently follows the administration of nicotinic acid and sodium nicotinate.

From 3 to 5 mg. of riboflavin, administered orally in tablet form or intravenously in sterile physiologic solution of sodium chloride, is effective for the average case of riboflavin deficiency. Since riboflavin is not very soluble in saline solution, the oral method of administration is recommended.

Very little is known concerning either the maintenance requirement or optimal dosage for vitamin K. Early work indicates that maximal prothrombin response is obtained when the crude vitamin extracted from 300 Gm. of alfalfa is given orally over a period of from three to four days. Recent work has shown that the oral administration of from 1 to 5 mg. daily of 2-methyl-1, 4-napthoquinone usually will give excellent results, though for some cases this amount will have to be increased. Since complete absorption is dependent on the presence of bile in the intestine, it is necessary, when vitamin K is administered orally, to give bile or bile salts along with it, as for example in cases of obstructive jaundice. Satisfactory results are obtained if the daily dose of the vitamin is emulsified in from 1 to 2 ounces (30 to 60 cc.) of bile or is given with a comparable amount of animal bile salts.

The intravenous injection of 50 mg. of vitamin B_6, dissolved in sterile physiologic solution of sodium chloride, is effective in the treatment of symptoms of vitamin B_6 deficiency. Evidence indicates that vitamin B_6 will relieve, at least temporarily, certain other conditions as described in the section on vitamin B_6; but, since response is not uniformly observed in all cases, its use is not recommended until further study has been made.

Vitamin E (synthetic alpha-tocopherol) in sterile oil, injected intramuscularly in dosage of 500 mg., relieves temporarily the symptoms of weakness and pain in the legs. In some cases a second injection of 500 mg. may be required.

Because of the severe reactions produced by the intravenous administration of adenylic acid, its use is not recommended.

Stanbery, Snell and Spies have shown that the content of pantothenic acid in the blood and urine is from 23 to 50 per cent lower in persons having pellagra, beriberi and riboflavin deficiency than in normal persons.

In the mild and moderately severe cases of mixed deficiency disease, dry powdered brewers' yeast (from 75 to 100 Gm.), liver extract (from 75 to 100 Gm.) or wheat germ (150 Gm.) daily should be given orally as supplements to the diet. Yeast and wheat germ have an advantage over the pure chemical substances in that they contain nicotinic acid, vitamin B_1, riboflavin and vitamin B_6, as well as minerals, proteins, enzymes and salts, and probably still other as yet unknown essential factors. A strain of yeast, designated C-50, furnished

by Anheuser-Busch, Inc., for experimental purposes, has been found more palatable than the other strains we have used. Many of the patients who objected to the taste of brewers' yeast will take it without complaint when it is combined up to 25 per cent with peanut butter or catsup.

SUMMARY AND CONCLUSIONS

During the past year and a half, 1,500 persons with clinically associated deficiency disease syndromes have been treated without a death. (The death rate from severe pellagra alone a few years ago was often as high as 54 per cent.) Our studies indicate that these people have a mixed rather than a single deficiency disease, and from a practical standpoint the response of these persons indicates that mixed vitamin therapy is often desirable. We recommend the administration of water-soluble vitamins together, rather than individually, and fat-soluble vitamins together, rather than individually, as having a definite usefulness in the treatment of deficiency diseases. Even when specific therapeutic agents are administered in the treatment of deficiency diseases, persons of all ages should also be given a well balanced, high caloric diet.

Special Article

CONFERENCES ON THERAPY

THE TREATMENT OF BLOOD DISORDERS

IX. POLYCYTHEMIA, HODGKIN'S DISEASE AND SPLENIC DISORDERS

NOTE.—*These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with the collaboration of other departments and institutions. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Treatment of Blood Disorders: X. The Disorders of the Blood Produced by Drugs and Their Treatment."*

DR. PAUL REZNIKOFF: Polycythemia vera, or erythremia, is due to an increased production of red blood cells. There is not complete agreement as to the cause of this increased production, and the various suggestions which have been made have contributed little to treatment. The aim is either to inhibit production or increase destruction, so that the red blood cells tend to approach normal. Of course there are many ways of doing that, but today I wish to speak only of the four accepted methods of treatment, by which I mean methods that have been tried and found effective and which can be used over long periods of time. Different patients respond differently to the various methods. What is good for one patient is not good for the other, and the customary procedure is to try first the method which the clinic customarily uses and see how the patient reacts to it.

Let us consider first irradiation. The methods vary a good deal. Some workers like to use "spot" irradiation; that is, irradiation of the bone marrow, the spleen or both. That works pretty well. The unitage varies, but commonly 50 roentgens is given at each treatment and the location is varied: at one time over the sternum, at another over the long bones or over the spleen, and so on. Sometimes spot irradiation is used when a patient has pain due either to perisplenitis or to pressure symptoms from a large spleen; but there is not very good evidence that irradiation over the spleen causes much regression of its size or changes the intensity of the symptoms.

Another method is "spray" irradiation. It is effective and well tolerated. We have given as much as 50 roentgens three times a week for from three to six treatments, after which a blood count is taken as a check on the changes produced.

The second method which is used is a hemolytic agent, one which probably has also some depressing effect on the bone marrow, a phenylhydrazine derivative. We believe the least toxic of these is acetylphenylhydrazine. Our usual dose at first is 0.1 Gm. in a capsule. A patient coming in with a count of 10,000,000 red blood cells will be given 0.1 Gm. of acetylphenylhydrazine once a day for about a week; if the patient has to leave the hospital, we usually give this dose every other day. Then we take red blood cell counts once a week, and as the count falls we decrease the dose and try to determine the amount which will maintain a reduced cell concentration and keep the patient comfortable. As a rule patients with polycythemia do not have symptoms from the polycythemia alone. Although each patient is more or less a rule in himself, in general we try to maintain the red cell count at approximately 5,500,000. Actually it is found that some patients will be kept for long periods with a fairly normal count on 0.1 Gm. of acetylphenylhydrazine a week, while others will require this dose every other day.

The third treatment which is effective in polycythemia is solution of potassium arsenite. Those of you who want to get the details of this might read an article by Drs. Forkner, Scott and Wu, published in the *Archives of Internal Medicine* in 1933. There is no question that solution of potassium arsenite will act effectively and can be used over long periods. We have not used it much for polycythemia in our clinic, employing instead a hemolyzing agent, usually acetylphenylhydrazine. We have had good results with that and x-rays, but solution of potassium arsenite will doubtless accomplish the same results, although I think its mechanism is different. It exerts a direct action on the bone marrow and is a regulator of red blood cell formation rather than a depressant. Is that about your point of view, Dr. Forkner?

DR. CLAUDE E. FORKNER: Yes, I think it tends to put cell production up or down.

DR. REZNIKOFF: That is the reason I called it a regulator. We discussed the dosage of solution of potassium arsenite in connection with the treatment of myelogenous leukemia, and its use in the treatment of polycythemia is about the same.

Not one of these three methods of treatment gives immediate relief. It is perhaps ten days or two weeks before the blood count begins to decrease. Some patients have headaches, dizziness and hemorrhages, and it is desirable to do something immediately for those individuals. In such a case there is no better procedure than phlebotomy. Stephens at Rochester studied the question carefully and he believes that phlebotomy at stated intervals does not affect the bone marrow deleteriously; that is, it will neither depress it nor tend to stimulate it. We had a patient who used to come to the hospital from out of town once a month for a phlebotomy, and that is the way he was treated for a period of five years. His blood count remained fairly normal and he felt comfortable. Dameshek, of Boston,

combines phlebotomy with low intake of iron. The rationale for that is not clear. It seems to me that most of these patients have a fairly normal color index and I do not understand why cutting the iron down inhibits cell production because we know that in iron deficiency anemia the red cell count is very often normal.

Those are the four methods of choice and we often combine them. There are questions that sometimes arise: Shall we use polycythemic blood for transfusion? I do, other things being equal. I don't think Dr. Forkner is keen on it, but we have used it several times and so far have not seen any bad results.

There are many other methods for the treatment of polycythemia, but those are the four in most general use. Formerly benzene was used, and I think some people still use it. Perhaps if we did not get such good results with the other methods we would go back to benzene. On the other hand, benzene may also depress platelets and white blood cells, and we want to avoid that. The toxic effects of acetylphenylhydrazine have not been observed in our clinic. The only patient who gave us concern was a man who became markedly jaundiced, and we are not sure but that he had some liver damage to start with.

I should like to emphasize that in addition to treating the blood in polycythemia you must treat the patients. In the first place, these people are likely to have vascular changes and often are high strung, nervous and irritable. They are usually difficult, and you have to treat the emotional factor.

As far as possible you should avoid putting patients with polycythemia to bed, because they are prone to develop thrombosis and it is better to keep them fairly active. These patients also have marked congestion of the mucous membranes, so a diet must be selected which will minimize the possibility of irritating the membranes. I tell them that they should avoid condiments, too much rough food and foods or drinks at too high a temperature. Concentrated alcoholic drinks should also be avoided. These general factors are important.

TREATMENT OF HODGKIN'S DISEASE

DR. FORKNER: Dr. Craver will tell us about the treatment of Hodgkin's disease.

DR. LLOYD F. CRAVER: The great dispute, of course, is as to whether Hodgkin's disease is to be regarded as an inflammatory process or as a neoplasm. I think the general tendency is to regard this disease, at least in its early and intermediate stages, as an inflammatory process, probably caused by various stimuli of the lymph node system, chief among which is tuberculosis. There certainly is much clinical evidence, though perhaps not so much laboratory evidence, that tuberculosis may play a large part in the etiology of Hodgkin's disease. We look on it as a process which gets its beginning as an inflammatory overreaction on the part of the lymph node structures to these various stimuli, whatever they may be, among which the most important may be tuberculosis; a process which, once established, goes on of its own momentum and which in certain cases may go on further to a condition which at least resembles a true neoplasm, Hodgkin's sarcoma.

There is not a great deal to say about the treatment of Hodgkin's disease except to talk about irradiation because, despite the various efforts that have been made along other lines, irradiation remains the chief resource. In many instances it is worth while to treat these patients even in advanced stages, because no matter how bad a case looks you may seem to drag the patient back almost from the brink of the grave by irradiation, provided you have been fortunate in choosing your doses, the intervals between treatments and the areas treated.

With Hodgkin's disease, as with all the lymphomatous processes, one finds that there is no region of the body that is entirely immune from being involved in one way or another. Therefore Hodgkin's disease and the other lymphomatous processes as well are conditions that should be familiar to all practitioners of medicine, whether they are dermatologists, obstetricians, neurologists or what not. These are some of the main complications that were found in a series of 220 cases: lesions of the lung 29 per cent, pleural effusions 17 per cent, ascites 8 per cent, jaundice 6 per cent, itching 29 per cent, various cutaneous lesions 13 per cent, various neurologic lesions 12 per cent, lesions of bones 18 per cent. I firmly believe that all those complicating symptoms and lesions would give a higher percentage if we had followed all the 220 cases all the way through. Lesions of the bone, for example, which are detectable roentgenographically I believe might be found under modern conditions in perhaps as many as 45 or 50 per cent of all cases of Hodgkin's disease. Under modern conditions of radiation therapy, when the patients do not die of mediastinal pressure or other features from which they perhaps did die years ago they are possibly kept alive long enough to have more of these complications. As for the neurologic lesions, you will find in the literature cases in which operation has been performed for supposed primary spinal cord tumor, the operation revealing Hodgkin's disease, which was not primary there but gained entry to the spinal canal along the intervertebral foramens.

Hodgkin's disease may produce lesions in the lung simulating sarcoma metastases. In general, when a patient with Hodgkin's disease has that amount of lung infiltration the outlook is pretty bad; yet at times it is possible to clear it up satisfactorily, at least temporarily, by irradiation. We have had several cases in which a lung abscess has formed apparently as a result of bronchial blockage and retention of secretions and breaking down of lung tissue, and two instances of tracheo-esophageal fistula.

As an illustration of another type of intrathoracic Hodgkin's granuloma, I might cite a young woman presenting a bulky intrathoracic mass filling one side of the chest. Looking at her chest film, one might think the mass grew out from the mediastinum or at least from lung infiltration, but after irradiation there was a residual nodule on the inner surface of the chest wall, and spot films of the ribs showed that three or four ribs were grossly involved by an osteolytic process. This patient survived about six years after the disease began. She had about every conceivable complication. At one time she had complete paraplegia below about the ninth dorsal level. She could not even wiggle her toes. That was after she had been under treatment for two years. Heavy irradiation given promptly over the appropriate level in the spine resulted in her being able to walk within a month or six weeks, and she was up and around for two years after that before her terminal state.

The type of bone involvement most commonly seen complicating Hodgkin's disease is an osteolytic process, often found in ribs, sternum, vertebrae, pelvis, humerus or femur. A more uncommon type of bone lesion in Hodgkin's disease is the osteoplastic variety, likely to involve more than one bone especially vertebrae, pelvis and femurs. In some cases one bone, as a single vertebra, may show osteoplasia. This type of lesion is usually accompanied by rather vaguely defined pains

over a large field about the involved bones, and it may be relieved, at times very well and at other times less satisfactorily, by irradiation. I think that in general the osteoplastic type shows less relief from pain after irradiation than does the osteolytic type.

Often it is difficult to tell whether one is dealing with a little variation in the roentgenographic technic or an actual osteosclerotic process. Blood phosphatase levels seem to be fairly well correlated with the bone lesions, especially in Hodgkin's disease, although not too closely. There are very high phosphatase levels, in some cases up to 35 and 40 units per hundred cubic centimeters (Bodansky).

A rare condition is ulcerating Hodgkin's granuloma in the skin. The girl I mentioned who had the massive chest involvement and paraplegia had a cutaneous granuloma behind her left ear simulating a sebaceous cyst. It did not contain pus on incision and cleared up promptly after a single low voltage roentgen treatment.

Now there are many different principles used in the irradiation of Hodgkin's disease. Some like to use large doses, some like small doses; some like to irradiate large fields, others prefer small fields. I think there is a certain scope for total body irradiation in Hodgkin's disease. The general practice among most roentgenologists in giving local irradiation is to use a fairly small dose at a time, not over 100 or 200 roentgens. Some years ago we were in the habit of using rather large doses, in the order of from 400 to 600 roentgens at a single exposure, and we have the impression that some of our patients that have done the best have been those treated by that method. I do not think that we would want to put ourselves in the position, however, of recommending large doses, singly or repeated a few times, as the routine method. I think the treatment in Hodgkin's disease has to be greatly individualized. As an example of the method of heavy doses at a sitting, a patient treated in 1931, whose disease was limited apparently to each side of the neck, never had any evidence of mediastinal involvement or generalization of the process. We treated his neck repeatedly by heavy single doses of about 400 or 500 roentgens at intervals of three or four weeks. He now has some radiation changes in his skin and a certain amount of atrophy and dryness but no breaking down. He has been working continuously and is in excellent condition at the present time, with complete regression of the disease.

Our proved cases of Hodgkin's disease show a five year survival of 17 per cent, a figure considerably lower than that reported by some workers. Gilbert in Switzerland reports 34 per cent five year survivors, but I feel that his patients must come to him in considerably earlier stages on the average than ours do because a great many of our patients who have been treated a good deal elsewhere are sent to us as difficult problems. I believe that for 17 per cent to survive five years is not bad considering the type of cases we receive.

As far as other methods of treatment are concerned, transfusions are of value to put the patient in better physical condition so that he may tolerate further irradiation. Iron is also of value at times. It is important to have the patient carry out a regimen as for tuberculosis, with rest and fresh air, moderate exposure to sunshine and a good nutritious diet. Other than that, there is not much to be done.

The problem of itching becomes troublesome at times. It is best relieved by treating the active Hodgkin's disease if you can find it. A patient whom I first saw about a year ago had a bulky mediastinal mass. Biopsy of a neck node showed a rather active type of Hodgkin's disease, almost Hodgkin's sarcoma. She had such severe itching that she was covered literally from head to foot with long deep scratch marks. She had been treated by a dermatologist and had been seen in consultation by a hematologist, who advised against treating the mediastinal mass, apparently because he believed that it was so active that it might be aggravated by treatment or that she was going to die soon anyway; but she did not die. She fussed along for a year, getting a little roentgen treatment for the skin and various salves and lotions with no benefit. I decided to ignore the skin condition but to irradiate the mediastinal mass. Within three weeks the itching stopped entirely. The skin lesions cleared up after a few months, and she has gained about 20 pounds (9 Kg.). So the principle in treating itching is to find the active Hodgkin's disease and treat that. The various dermatologic measures do not do much good.

DISORDERS OF THE SPLEEN

DR. FORKNER: The treatment of some splenic disorders is discussed by Dr. Andrus.

DR. WILLIAM DEWITT ANDRUS: Splenectomy has come to be a well recognized part of the treatment of certain disorders of the blood and blood forming organs, notably congenital hemolytic jaundice, thrombopenic purpura and Banti's disease, although we must admit that both the role played by the spleen in the production of these disease pictures and the exact factors which bring about improvement after its removal are not clear.

Congenital hemolytic jaundice, representing the purest type of chronic hemolytic anemia due to intrinsic factors, is characterized by increased fragility of the red cells in hypotonic salt solution and by spherocytosis, reticulocytosis, splenic enlargement and a positive indirect van den Bergh reaction.

In the light of present knowledge of the role of the spleen in the destruction of red cells its removal would seem definitely indicated in this condition, in which the cells are abnormally fragile. It should be remembered, however, that the destruction of red blood cells is a function of the reticulo-endothelial system, in which the spleen plays a dominant role because of the concentration of a large portion of the elements of this system in that organ. By removing the spleen, therefore, we remove only a portion of the cells responsible, but fortunately a sufficient portion to restore a more nearly normal balance between blood formation and blood destruction in most cases.

In a typical case the indications for splenectomy are obvious and overwhelming, and the question resolves itself into selecting the optimum time for operation. As a rule it may be said that one should avoid operation when the patient is going into a hemolytic crisis and perform splenectomy as the crisis is receding or in a free interval. This is not always possible, however, as the crises may be very severe or recur so frequently as to leave little choice. In general the patients stand the operation well, as the spleen, though often much enlarged, is seldom adherent and can usually be removed quite easily.

More debatable is the question of splenectomy in patients who have the disease in a latent form, many of whom undoubtedly may go on for years or even throughout life without showing acute symptoms. Such patients should be kept under close observation, and operation should be advised if any tendency to abnormal hemolysis is noted, as even a very long period of free-

dom from symptoms is no guaranty of their continued absence. In one of our patients acute symptoms developed at age 58, including anemia with a count of 1,600,000 red cells but fortunately with a very high reticulocyte count. She stood operation well and has made an uneventful recovery.

The results in the eighteen cases of familial hemolytic jaundice in our series have all been good. There have been no operative deaths, and with the exception of one patient who died of pneumonia after four years and a boy in whom portal thrombosis developed three months after operation, all are living and well.

Thrombocytopenic purpura, of which there were fourteen cases in our series, is characterized by purpura, spontaneous hemorrhages and a marked decrease in the number of platelets in the circulating blood. The bleeding time is prolonged and the clot shows poor retraction. Changes in capillary permeability also play a role. The suggestion has been made that the disease really involves the entire reticulo-endothelial system.

Splenectomy is now recognized as indicated and gives excellent results in the typical cases associated with definite thrombopenia. However, the high mortality in the acute cases in the earlier reported series—as high as 87 per cent in some reports—compared with the apparent safety of the operation in the chronic type of the disease led surgeons and internists alike to condemn splenectomy in the acute stage. This mortality has been steadily falling, however, and some of the most brilliant results have followed early operation. However, it must be said that patients with the disease in the acute form are not good operative risks, and that fact will deter surgeons from operating on them except as all other measures fail.

Various medical measures, particularly repeated blood transfusions, may arrest the hemorrhage or even bring about an enduring remission of the disease in some cases, and the injection of ascorbic acid is sometimes capable of producing remarkable improvements or remission. However, in many cases even these measures fail to stop the bleeding entirely or to restore the blood picture to normal, and they but rarely produce the really spectacular results which often follow operation.

There were no deaths from the operation in our group, although one patient died five months after operation with persistent thrombopenia and anemia. It is possible that we were mistaken in our diagnosis and that she should have been classified as having aplastic anemia. Another patient died with agranulocytosis precipitated by aminopyrine three years after splenectomy. All the remainder are well and have practically normal red cell counts from six months to four and one half years after operation. The platelet counts are known to be normal in all except one, who has not been back to the follow-up clinic. She writes, however, that she is free from her symptoms. One patient had a high platelet count at the time of the last observation.

With regard to Banti's disease (splenic anemia), although Greisinger is said to have used the term "splenic anemia" in 1866, it was Banti in 1883 who first gave impetus to the study of this condition, and Osler from 1900 to 1902 added to our knowledge of the clinical picture. Banti described the disease as characterized by progressive splenomegaly, anemia of the microcytic type, leukopenia, slight thrombopenia and hematemesis, progressing to obvious cirrhosis of the liver with jaundice and ascites. He also considered phlebitis of the portal vein as a uniform feature of the disease. There is doubt as to whether the primary disease is in the spleen or the liver.

The removal of the spleen in this condition seems definitely warranted in the early stages and may alleviate some of the symptoms over a considerable period. The benefit which results would seem to be due to the reduction of the amount of blood coming to the liver through the portal vein which follows splenectomy. However, the operation is attended with certain risks, since the spleen is commonly adherent and has developed a collateral circulation at its upper pole which may be difficult to handle. Further, in many of the patients the platelets reach very high levels after operation and thromboses are not uncommon. Indeed, if one accepts the criterion of an unexplained febrile course as possibly indicating thrombosis, this complication would seem to be quite common in this disease.

There were no operative deaths in our series of ten cases, but two years after operation one patient died of progressing cirrhosis with ascites. The longest time which has elapsed since operation is three ond one half years, and three additional patients have suffered recurrence of hemorrhage.

In general, the operative mortality is higher in this condition than in either of the foregoing and the results less satisfactory. Pemberton reports 167 splenectomies for this condition with sixteen deaths. The remaining 151 patients were followed for as long as twenty-two years, and fifty-two of them had died—more than one third from recurrence of hemorrhage. Similar study of 118 operations for hemolytic jaundice showed four operative deaths and only seven additional fatalities occurring during the follow-up period.

COOLEY'S ANEMIA

We have performed splenectomy in six cases of Cooley's anemia—the peculiar anemia of childhood which occurs apparently only in children of Mediterranean parentage. The youngest was less than 6 months and the oldest 6 years of age. There were no operative deaths, but two of the patients have since died, one eight months and one two years after operation. There is no evidence that splenectomy cures the condition, and the best that can be said is that the patients seem somewhat improved.

In conclusion it should be said that the results of splenectomy in congenital hemolytic jaundice and thrombocytopenic purpura as well as in selected cases of Banti's syndrome amply justify its use but that attempts to expand the indications beyond these three conditions are fraught with danger and in addition give very poor results for the most part.

DISCUSSION OF QUESTIONS

DR. FORKNER: First, I should like to ask Dr. Reznikoff what he considers to be the polycythemic level of red blood cells. We frequently find patients in the wards with counts of 5,500,000, of 5,800,000 or even of 6,000,000, and one immediately jumps to the conclusion that this is polycythemia vera.

DR. REZNIKOFF: In general if a male patient has a count under 6,000,000 and no symptoms, we don't pay much attention to it in our laboratory, especially if the hematocrit reading is normal. If the count is between 6,000,000 and 7,500,000, we usually term that an erythrocytosis analogous to leukocytosis. There should be very few symptoms as a result of an increase up to 7,000,000 or 7,500,000. Above 7,500,000, especially with a concomitant increase in the hematocrit level, we speak of erythremia, which is analogous to

leukemia and is more likely indicative of polycythemia vera. Of course, we see patients with polycythemia vera, as judged by later counts, who have a normal number of red cells, especially those who have been treated, so we cannot make the diagnosis of the disease on the basis of the blood count alone.

DR. FORKNER: Normal males not infrequently have blood counts as high as 6,000,000.

DR. HARRY GOLD: Theoretically, it would seem to me that arsenic, if it is effective, might be more desirable than phenylhydrazine because, as I understand, arsenic suppresses the red cell formation whereas phenylhydrazine exerts its action by destruction of red cells. The products of destruction of red cells produce undesirable effects. I believe that the kidneys sometimes rebel against some of the decomposition products. The tubules get into trouble.

DR. REZNIKOFF: I think that our patients, some of whom have been treated for eight and nine years with acetylphenylhydrazine, do not show evidence of damage to either the liver or the kidneys. They are able to work without difficulty.

DR. FORKNER: With further reference to the use of arsenic I might say that this substance will bring a red count down from almost any level to normal. It is difficult to push the count below normal with arsenic, but on the whole it is more difficult to get a satisfactory response with solution of potassium arsenite than with either x-rays or phenylhydrazine. In choosing an agent for treatment I would put solution of potassium arsenite as third choice. We employed it because we were interested in the mechanism of the effects of arsenic. We found that it works in pernicious anemia, in polycythemia and in leukemia. Just how it works we do not know, but it does depress the bone marrow. On the other hand, phenylhydrazine stimulates the leukopoietic tissue of the bone marrow.

DR. GOLD: Is it stimulated by the phenylhydrazine directly or by the products of the destruction of red cells?

DR. REZNIKOFF: There is evidence of a stimulation of the leukocytes even without treatment. The disease itself causes a stimulation.

DR. FORKNER: But they go higher with phenylhydrazine, don't you think?

DR. REZNIKOFF: That is true in a certain number of these patients; some go over into leukemia.

DR. FORKNER: There is another point in connection with the use of phenylhydrazine in polycythemia, and that is it may cause thrombosis, particularly in older patients. It is a capillary toxin.

DR. REZNIKOFF: Has that been your experience?

DR. FORKNER: Yes.

DR. REZNIKOFF: We find the incidence of thrombosis just as high in untreated patients.

DR. MCKEEN CATTELL: To the extent that these conditions occur in children, I wonder whether they present special problems in treatment. Cooley's anemia, mentioned by Dr. Andrus, belongs to this group.

DR. CARL H. SMITH: A problem that has come up recently concerns the adequate treatment of Cooley's anemia. The separation of erythroblastic anemia from the miscellaneous group of von Jaksch's anemia by Cooley has brought to light many children suffering with this disease. As pointed out by Dr. Andrus, Cooley's anemia with few exceptions is limited to children one or both of whose parents were born in Mediterranean countries, especially Italy, Greece or Syria and most frequently Sicily. For that reason the designation Mediterranean anemia or thalassemia has been suggested by Whipple and Bradford. The outstanding characteristics of this disease are not alone its racial but also its familial tendencies, the skeletal changes and the appearance of large numbers of circulating normoblasts. Undoubtedly the disease is transmitted as a recessive characteristic, but no instance has as yet been recorded of its transmission by an adult with the active form of this disease. While severe cases begin in early infancy, milder cases pass unrecognized until later childhood. There is evidence that, like hemolytic jaundice, the disease may be latent in healthy members of the family so that inheritance is a possibility. It is also possible that in this country there are many with mild or latent forms of this disease who may perhaps be suffering with an unexplained low grade chronic anemia.

The child with the active form of this disease shows a pronounced splenomegaly, a lesser degree of liver enlargement, frontal and parietal bossing, prominent malar eminences, slanting eyes, a muddy yellow complexion and icteric scleras. All these features combine to give these children a mongoloid appearance and account for the well known resemblance of the affected children to one another rather than to their normal sisters and brothers.

The blood shows a moderate to severe anemia, leukocytosis, reticulocytosis, an elevated icteric index, numerous nucleated red cells, which are remarkably increased following splenectomy, and a striking resistance of the red cells to hypotonic saline solution in fragility tests. X-ray study of the skeletal system reveals the evidence of the extreme hyperplasia of the bone marrow by osteoporosis, thinning of the cortex, trabecular atrophy, and thickening of the skull which is first observed in the frontal bones. Lateral views of the skull show an enlarged diploic space which is either finely granular or mottled, or striated, the latter giving the appearance of hair standing on end.

With the earlier recognition of the condition by the roentgenogram, blood studies and its suspected recurrence in an affected family, we now have under observation in our clinic a fairly large group of infants and young children with this disease. The problem with which we are confronted is what procedure to follow, not in the moderate or advanced cases that come to you, Dr. Andrus, for splenectomy, but for the mild and early cases we have been able to uncover. Should splenectomy be reserved for cases in which the weight and pressure effects of the greatly enlarged organ seriously inconvenience the child, or should the spleen be removed when the disease is first recognized, before it has become large, before the liver undergoes enlargement and before extensive skeletal changes set in? It is entirely probable that splenectomy prolongs life, and this is strikingly illustrated by the patient of Stillman and Hitzrot, who lived eighteen years after the operation. We are now following a small group of infants on whom splenectomy was performed in early infancy. While it is too early to arrive at any conclusion, splenectomy seems to have retarded the disease, but the choice of cases and optimal period for this operation await further study.

Since the disease is only in part hemolytic and is probably due fundamentally to a deficiency of unknown hemopoietic principles or to a metabolic disturbance, splenectomy can be expected to modify the disease but slightly. Where the hemolytic activity is extreme, however, splenectomy is most benefical. In our experience

one of the prime benefits of this procedure has been the reduction of the number of transfusions required to maintain life. It is often difficult to obtain and transfuse blood at biweekly intervals, as is sometimes necessary in the severe cases in infants and young children. In some of our cases in which this need existed, splenectomy has succeeded in lengthening the interval between transfusions. We are endeavoring at present to determine the level at which children with this disease can live comfortably without transfusion.

DR. HENRY B. RICHARDSON: Can you tell whether this is an anthropologic group or a geographic group?

DR. SMITH: We know little about the anthropologic aspect of this disease. At present it cannot be stated whether there is any one race which posseses this recessive character. While with few exceptions this disease is limited to children of Mediterranean parentage, it has been pointed out by several observers that inhabitants of these countries represent an admixture of races. During the reign of Alexander the Great, for instance, the Greeks colonized the Mediterranean countries extensively, and it has been shown that the southern Italians with this disease are in part of Greek origin. Caminopetros in Greece has recently pointed out that some of the settlers about Athens have originated from Asia Minor and that they represent a mixture of many races with the Mongolian. Among the parents and grandparents of children with erythroblastic anemia, he has observed individuals with characteristic Mongolian eyes. It should be emphasized, however, that the Mongolian appearance of these children is in reality produced by skeletal changes in this disease.

DR. CRAVER: Have you found any in the Negro race?

DR. SMITH: I know of no instances of this disease among Negroes.

DR. ADE T. MILHORAT: Does roentgen treatment influence the bony lesion?

DR. SMITH: X-rays do not modify this disease. There is no specific treatment for it. Iron, copper, liver, extracts of glands and of other organs, and vitamins have been employed without success. At the suggestion of some observers that the disease may represent a congenital form of malaria, we have employed quinine, but again without results.

DR. FORKNER: Excessive irradiation can produce purpura.

SUMMARY

DR. GOLD: The diagnosis of polycythemia vera does not depend on the blood count alone. However, symptoms are likely to appear at red cell count levels of about 7.5 million, especially when the hematocrit is increased. The more specific measures in treatment are directed to the reduction of the red cell count. This is achieved most rapidly by phlebotomy, which gives immediate relief from such symptoms as headaches, dizziness and hemorrhages. Acetylphenylhydrazine appears to be the most effective chemical agent for reducing the red cell count. Its mode of action is to destroy red cells in the circulation. Arsenic in the form of Fowler's solution may also restore the red cell count to normal, but it is generally less effective than acetylphenylhydrazine in polycythemia vera. Its mode of action is different and appears to be through an influence on the erythrogenic function of the bone marrow rather than by destruction of red cells. Reduction of the red cell count in polycythemia vera may also be accomplished satisfactorily by irradiation, which may be applied either by the spot or by the spray method.

With regard to Hodgkin's disease, the view has been expressed that in the early stages it is probably an inflammatory process in the lymph node system, which later acquires a growth momentum of its own. Practically every system of the body may be involved in Hodgkin's disease, giving rise to lesions in the lungs, pleural effusions, ascites, jaundice, itching, cutaneous lesions, neurologic lesions and involvement of the bones. The treatment of Hodgkin's disease is essentially a matter of suitable irradiation. The lesions are quite sensitive to radiation therapy and marked improvement is often obtained in some of the most advanced and seemingly irreversible stages of the disease with appropriate treatment which involves suitable doses, intervals and areas of application. The details of the use of irradiation in this disease, which have been discussed by Dr. Craver, need not be rehearsed. Suitable radiation therapy not only causes the lymph node masses to diminish in size or to vanish but improves the patient's general health. One instance of severe pruritus was cited in which the treatment of the mediastinal masses resulted not only in their disappearance but in the cessation of the intractable itching.

We have had a brief account of the use of splenectomy in disorders of the blood and blood-forming organs. It appears to be an effective therapeutic measure in the relief of congenital hemolytic jaundice, thrombocytopenic purpura, Banti's disease and possibly Cooley's anemia. Dr. Andrus and Dr. Smith have outlined the essential differential characteristics of these diseases and the indications for splenectomy.

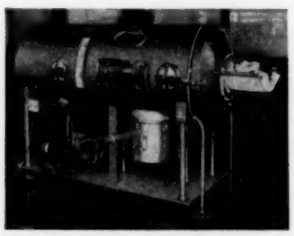
Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

COLUMBIAN RESPIRATOR ACCEPTABLE

Manufacturer: Columbian Steel Tank Company, 1401-1621 West Twelfth Street, Kansas City, Mo.

The Columbian Respirator produces artificial respiration simulating natural breathing for indefinite periods of time. The respirator applies a new principle for controlling vacuum and pressure which is described as a "liquid sealed air pump."



Columbian Respirator.

A cylindric steel chamber containing a removable bed is mounted on a framework, which also supports the operating mechanism. A one-sixth horse power motor operates the unit on direct or alternating current. It is possible to obtain within the chamber a maximum positive pressure of 15 cm. and a maximum negative pressure of 15 cm. The respirator is 56 inches high, 80 inches long and 32 inches wide, and the shipping weight is approximately 1,300 pounds.

The chamber of the respirator is available on the one side through three 5 inch diameter rubber sealed hand ports, and on the other through two hand ports and one bedpan door 6 inches wide by 16 inches long. The interior is illuminated by an electric light. On each side of the respirator is a chrome framed viewing window made of unbreakable cellulose acetate. The bed assembly is supported on large roller casters so that it can be pulled full length out of the respirator shell. The bed frame is hinged and a hand screw outside the respirator permits raising and lowering the patient's shoulders. A

mattress made with "kapok" filler and transparent waterproof cover is standard equipment.

In operation, the patient is placed on the bed, which is extended full length out of the shell, a sponge rubber neck seal is pulled over the head, and the bed is rolled into the respirator. Two hand screws are tightened, and the patient's body is sealed within the chamber. The head remains outside the respirator, lying on a pillow, which is supported by an adjustable canvas swing which can be raised or lowered by removable solid arms. The neck seal is held in place by a self-centering neck ring and three hold down clamps.

The liquid sealed air pump, a feature of the mechanism, consists of two telescoping tanks. A chrome tank, open at both ends, is bolted to the body of the respirator and fits within another tank of stainless steel which holds a narrow ring of liquid, preferably a solution of water and glycerin. A rocker arm raises and lowers the outer tank, creating a liquid sealed vacuum in the stationary inner tank; this results in a movement of air in and out of the body of the respirator. The alternate vacuum and pressure causes the chest to rise and fall as in normal breathing. In clinical use it was reported that the pump was quiet in operation. The volume of vacuum and pressure is controlled by inlet and outlet valves of the body of the respirator, and an adjustable arm permits the length of the piston stroke to be changed. A speed changing pulley provides a range of from ten to thirty respiration per minute with a number of graduations. An auxiliary hand drive is provided for use in case of power failure or when electric power is not available. Operating the respirator by hand is automatic except for counting the number of crank turns per minute.

The amount of vacuum and pressure is read by a spring type centimeter gage. Located in the removable headpiece are the rubber pressure relief valve and plugged opening for the patient's signal line. The plugged opening is also used for administering intravenous solutions. A sliding gage attached to the base of the respirator and parallel to the sliding base of the motor is calibrated from 0 to 30 respirations per minute and is adjustable for retiming. The gage permits a quick determination of the respiratory rate.

The apparatus was referred by the Council to a qualified investigator for clinical use. He reports to the Council that the apparatus gave satisfactory service.

The Council voted to accept the Columbian Respirator for inclusion on its list of accepted devices.

FARIES S-4 SUNLAMP MODELS 2404-2455 ACCEPTABLE

Manufacturer: Faries Manufacturing Company, Decatur, Ill.

The Faries S-4 Sunlamp is designed to produce ultraviolet radiation within the limits of the standards set by the Council for devices using the term "sunlamp." These standards require that the energy of wavelengths shorter than and including 2,800 angstroms shall not exceed 1 per cent of the total energy of wavelengths between 2,804 and 3,132 angstroms. These wavelengths fall in the spectral region of low erythematogenic action and render the sunlamp suitable for unsupervised use by the layman.

Faries S-4 Sunlamp, Models 2404-2455

The source of ultraviolet energy, the S-4 bulb, is mounted in reflectors on adjustable supports. This S-4 bulb consists basically of a quartz mercury arc about 1½ inches long, enclosed in a special glass bulb which transmits ultraviolet wavelengths of 2,894, 2,967, 3,024 and 3,132 angstroms (and longer wavelengths) but which cuts off most of the wavelengths shorter than about 2,800 angstroms. The lamp produces the characteristic blue green light of the mercury line spectrum. The total power required is 120 watts; line, from 110 to 120 volts; the lamp operates only on alternating current.

Spectral ultraviolet radiation measurements were made on the S-4 lamp in a laboratory selected by the Council. These measurements showed that the radiation of wavelengths shorter than 2,800 angstroms is immeasurably small and hence these lamps qualify as sunlamps, so far as spectral quality (wavelength) of radiation is concerned.

In this investigation the lamp was placed close in front of the quartz-fluorite achromatic spectroradiometer, and the spectral intensities were measured with a vacuum thermopile. The relative spectral intensities (galvanometer deflections) corrected for absorption in the spectroradiometer are given in the accompanying table.

Relative Spectral Intensities

Wavelengths (Angstroms)	Relative Energy (Average of Three Lamps) Microwatts per Sq. Cm.
3,132	7.96
3,024	2.59
2,967	1.15
2,894	0.28
2,804	0.09
Total	12.07

The radiation at 2,804 angstroms (and shorter if measurable) is about 0.75 per cent of the total of all wavelengths, including 3,132 angstroms and shorter. Mounted in an aluminum reflector, the radiation at 2,894 angstroms and shorter, relative to the total, would be still lower; hence these lamps comply with the Council's requirements for acceptability of a sunlamp for spectral quality of ultraviolet radiation.

The Council on Physical Therapy voted to accept the Faries S-4 Sunlamp for inclusion on its list of accepted devices.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

AMPULS OF CAMPHOR.—"Ampuls of camphor contain a sterile solution of approximately 20 Gm. of camphor in a sufficient quantity of ampul oil to make 100 cc., unless another concentration of the solution is stated on the label, and yield not less than 93 per cent and not more than 103 per cent of the labeled amount of camphor." *N. F.*

For standards see the National Formulary under Ampullae Camphorae.

Actions and Uses.—Parenterally to sustain the circulation and respiration in collapse.

Dosage.—1 cc. containing about 0.2 Gm. of camphor.

Ampoules Camphor in Oil-Endo 0.2 Gm. (3 grains), 1 cc.: Each cubic centimeter contains camphor 0.2 Gm. (3 grains) in olive oil q. s.
Manufactured by Endo Products, Inc., New York.

Ampoules Camphor in Oil-Endo 0.2 Gm. (3 grains), 2 cc.: Each 2 cc. contains camphor 0.2 Gm. (3 grains) in olive oil q. s.
Manufactured by Endo Products, Inc., New York.

IRON AND IRON COMPOUNDS (See New and Nonofficial Remedies, 1940, p. 307).

SOLUTION OF FERRIC SUBSULFATE.—"An aqueous solution containing in each 100 cc. basic ferric sulfate equivalent to not less than 20 Gm. and not more than 22 Gm. of Fe." *N. F.*

For standards see the National Formulary under Liquor Ferri Subsulfatis.

Actions and Uses.—Local styptic and astringent.

Arzol Ferric Swabs: Cotton pledgets medicated with a solution of ferric subsulfate, N. F., 75 per cent; glycerin approximately 25 per cent and phenol 0.5 per cent.
Prepared by Arzol Chemical Co., Nyack, N. Y.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JULY 27, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

"SARCOIDOSIS"

Medical literature, particularly during the past four years, reveals a renewed interest in this disease of many eponyms. A research by Francis Hunter [1] into the history of its discovery has established that the first description of a case was given by Jonathan Hutchinson in 1869. Twenty years later (1889) Besnier described a similar case presenting the infiltrating type of cutaneous lesion, to which he gave the name "lupus pernio" (chilblain lupus). In 1899 appeared the important publication of Boeck, in which he described the nodular cutaneous lesions under the name of "multiple benign skin sarcoids" or "lupoids." Heerfordt, a Danish ophthalmologist, described in 1909 the syndrome presenting iritis or iridocyclitis in association with a febrile subacute swelling of the parotids and bilateral facial palsy. The identity of the two was recognized by Pautrier. Kuznitsky and Bittorf reported in 1915 a case of cutaneous sarcoid with evidence of morbid changes in the lymph nodes, spleen and lungs. Jüngling in 1919 described a roentgenographic entity presenting characteristic appearances in the digits and the metacarpal and the metatarsal bones, to which he gave the term "ostitis tuberculosa multiplex cystoides."

The clinical and the microscopic studies of the Stockholm dermatologist Schaumann,[2] however, first published in 1914, definitely established the essential identity of these apparently unrelated clinical entities. Schaumann pointed out that the disease may indeed exist in the absence of cutaneous lesions and that it displays a predilection for the lymph nodes, the tonsils, the bone marrow, the spleen, the liver and the lungs; in other words, for the organs of the reticulo-endothelial system. The most frequent and, from the clinical standpoint, the most important localization is in the lungs. Characteristic is the absence or paucity of signs elicited by percussion and auscultation when contrasted with the extensive pulmonary infiltrations revealed by x-ray examination.

The histologic unit, irrespective of localization, is a tubercle-like accumulation of epithelioid cells with occasional central necrosis but never caseation, a few Langhans giant cells and a ring of lymphoid cells. These foci show a pronounced tendency to fibrous and hyaline transformation. The lesion is essentially a granuloma closely resembling that of tuberculosis or of Hodgkin's disease but differing from the former in the absence of caseation and of tubercle bacilli. Because of the predilection for the lymph tissue and its essentially benign course, Schaumann gave it the more or less inclusive term "lymphogranulomatosis benigna." The cutaneous lesions present themselves as chronic painless infiltrations or nodules. There is in most cases a more or less universal, symmetrical enlargement of the lymph nodes. X-ray examination reveals in the great majority of the cases fairly characteristic hilar shadows extending fanwise into the lung fields. Striking also in the symptomatology is the wide dissemination of the lesions and the surprising mildness or absence of the symptoms. The patients may complain of fatigue and of rather considerable loss of weight. The course is usually afebrile, with only slight rises of temperature on the appearance of new lesions.

The cause of the disease has not been determined. A number of investigators, among them Schaumann, consider it an atypical anergic form of tuberculosis. The opponents of this theory, while admitting a close resemblance of lymphogranulomatosis to chronic miliary tuberculosis, point out certain differences, namely the absence of caseation, the failure to demonstrate either in stained sections, in cultures or in animal inoculations, tubercle bacilli [3] and negative reactivity to large doses of tuberculin (1 mg. and more). The proponents of

1. Hunter, F. T.: Hutchinson-Boeck's Disease (Generalized "Sarcoidosis"): Historical Note and Report of a Case with Apparent Cure, Brit. J. Dermat. **214**: 346 (Feb. 20) 1936.

2. Schaumann, J.: Sur le lupus pernio, Mémoire read before the Société française de dermatologie in November 1914; Lymphogranulomatosis Benigna in the Light of Prolonged Clinical Observations and Autopsy Findings, Brit. J. Dermat. **48**: 399 (Aug.-Sept.) 1936.

3. Harrell, G. T.: Generalized Sarcoidosis of Boeck, a Clinical Review of Eleven Cases, with Studies of the Blood and the Etiologic Factors, Arch. Int. Med. **65**: 1003 (May) 1940.

the tuberculous nature of the disease, however, regard the last phenomenon as anergy and urge in favor of their hypothesis the close morphologic resemblance, the occasional demonstration of tubercle bacilli, the fact that many of the patients eventually die of frank caseating tuberculosis, and the apparent mutual exclusiveness of sarcoids and tuberculous lesions. Thus, as observed in a number of instances, the sarcoid lesions disappeared with the development of a frank tuberculosis and the previously negative tuberculin test became positive. In some instances the removal of the tuberculous focus was followed by the return of sarcoids and a negative tuberculin reactivity. A number of investigators, among them Kissmeyer,[4] do not believe in the tuberculous etiology and regard such cases in the light of coincidental existence of two distinct entities. In view of the repeated negative bacteriologic studies, Kissmeyer believes that the disease is due to an unidentified virus.

METABOLISM OF IRON

Studies on the metabolism of iron are complicated by a number of physiologic variables beyond the control of the investigator. Iron exists in many combinations and in many places in the body, some of the most important being red cell hemoglobin, muscle hemoglobin, liver, spleen and marrow tissue. Further complications arise from the fact that in a single tissue the iron may exist in several different forms; in the spleen, for example, as iron in the parenchyma, as iron in the contained blood of the organ and as storage iron. Finally, and not unimportant in contributing difficulties to the problem, is the question of accurate quantitative determination of iron in tissues containing interfering minerals, e. g. salts of calcium and phosphorus. Again, the factors influencing the absorption of iron from the gastrointestinal tract, and the relation of the type of iron in the diet and the gastric acidity to this question, the mode of disposition of absorbed iron, the factors controlling the mobilization of iron by the organism, the iron turnover by various depots, the iron transport in the body and the excretion of iron are all problems of prime importance. They concern the understanding not only of the normal metabolism but also of iron metabolism in disease, notably anemia.

Through the medium of the cyclotron of the Research Laboratory at the University of California, radioactive iron has been made available for studies of iron metabolism. The bombardment of the iron isotope of mass 58 with deuterons generated by the cyclotron results in the formation of radioactive iron which decays with the emission of free electrons or beta rays. This radiation can be detected with a suitable physical apparatus and makes possible, therefore, a quantitative determination of radioactive iron. The time required for a loss of half the intensity of this radiation, the so-called half life period for radioactive iron, is forty-seven days, and this period is ample for the conduct of metabolic studies. The radioactive iron becomes a "marked" element which may be measured quantitatively in body tissues and fluids.

Investigators at the University of Rochester have been concerned for some years with the problems of hemoglobin formation, among which iron metabolism is of prime importance. With the aid of radioactive iron, these workers have now attacked the problems of the absorption, transport, utilization and excretion of iron both in the normal and in the anemic organism. One publication[1] deals with iron absorption; radioactive iron, in the form of ferric sulfate, was administered orally to normal dogs and to dogs made anemic by bleeding. The anemia was maintained for periods of from several weeks to several months by repeated bleeding and maintenance on a diet poor in iron. In the anemic animals, radioactive iron in amounts up to 9 per cent of the administered quantity was absorbed. The material in the colon and feces, when assayed for radioactive iron, accounted for up to 70 per cent of the administered isotope; the remaining unaccounted for iron can probably be charged to inefficiency of the methods of recovery used in the experiments. In striking contrast to the data obtained with the anemic dogs are the results yielded by normal animals; in the latter, little (less than 1 per cent) of the labeled iron was absorbed into the organism. The experiments establish the apparent ability of the dog to discriminate physiologically with respect to the quantity of iron absorbed from the gastrointestinal tract; when there is a distinct need, iron will pass from the intestinal tract into the blood stream. The magnitude of the body reserves of iron appears to determine the extent of the absorption of this element. Observations also indicate that iron absorption which does occur takes place in the small intestine and that the colon is not concerned with this process. The transport of iron from the intestinal tract to the various sites of utilization seems to be a function of the plasma. Within a few hours after its oral administration to anemic dogs the radioactive iron also can be demonstrated in the red blood cells.

In a second communication[2] the Rochester investigators have reported the results of a study of the excretion of radioactive iron after its intravenous injection as ferrous gluconate. Excretion of the iron was followed in the urine, bile and feces; an initial output was observed in urine and feces for a period (from three to fifteen days) following the iron injection and the quantity excreted accounted for from 2 to 8 per cent of the injected iron. Although the excretion of iron by way of the kidney subsequently dropped to values approaching zero, the feces contained measurable amounts of radioactive iron during the remainder of the experimental period. Blood destruction produced

4. Kissmeyer, A., and Nielsen, J.: Notes sur l'étiologie des sarcoïdes de Boeck, Acta dermat.-venereol. **14**: 283 (Oct.) 1933.

1. Hahn, P. F.; Bale, W. F.; Lawrence, E. O., and Whipple, G. H.: Radioactive Iron and Its Metabolism in Anemia, J. Exper. Med. **69**: 739 (May) 1939.

2. Hahn, P. F.; Bale, W. F.; Hettig, R. A.; Kamen, M. D., and Whipple, G. H.: Radioactive Iron and Its Excretion in Urine, Bile and Feces, J. Exper. Med. **70**: 443 (Nov.) 1939.

by an acetylphenyl hydrazine injection increased the fecal content of radioactive iron, the loss occurring for the most part through the biliary tract. In animals which did not show blood destruction, little fecal iron (0.01 mg. daily or less) is contributed by the bile. The evidence from these experiments indicates the difficulty with which the dog eliminates iron and supports the previous conclusion that the body controls its iron stores by regulation of absorption of iron rather than by the capacity of the organism to eliminate this element. The excretion of iron which does occur is chiefly by way of the biliary and gastrointestinal tracts in both the anemic dog and the animal with well stored reserves. McCance and Widdowson,[3] working with human subjects, concluded that the excretion of iron is so small as to be negligible and that the iron content of the body is usually regulated by control of absorption.

Progress in the problems of iron metabolism have been made possible by means of radioactive iron. It may be concluded on the basis of available data that the absorption of iron is regulated according to the needs of the organism, that absorbed iron is excreted at a low level but at a fairly constant rate in the feces, that this excretion can reach fairly high levels under certain conditions, and that the liver is in some manner concerned with secretion of iron through the biliary tract.

3. McCance, R. A., and Widdowson, E. M.: Absorption and Excretion of Iron, Lancet **2**: 680 (Sept. 18) 1937; The Absorption and Excretion of Iron Following Oral and Intravenous Administration, J. Physiol. **94**: 148 (Oct.) 1938.

Current Comment

BLOOD GROUPING TESTS IN EVIDENCE

Basing its conclusion primarily on the Report of the Committee on Medicolegal Blood Grouping Tests,[1] adopted by the House of Delegates in 1937, the United States Court of Appeals for the District of Columbia recently accepted as established the scientific value of blood grouping tests to the extent that they disprove paternity.[2] This case involved the paternity of a baby, born in wedlock. The trial court issued an order requiring the husband, the wife and the child to submit to blood grouping tests and this order was affirmed by the appellate court. Two questions were involved in the case: the right of the trial court to require submission to the tests and the evidential value of the results of the tests. The courts are, as a rule, hesitant to accept observations based on recently developed scientific processes. Perhaps this is as it should be, for often issues are involved that too vitally affect human relations to justify court determinations based on unstable experimental developments. One court has thus expressed the formula that should be applied in determining the acceptance, in evidence, of the results of the application of new scientific processes:

> Just when a scientific principle or discovery crosses the line between the experimental and demonstrable stages is difficult to define. Somewhere in this twilight zone the evidential force of the principle must be recognized, and while courts will go a long way in admitting expert testimony deduced from a well recognized scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field to which it belongs.[3]

The admissibility of the results of blood grouping tests has been before the courts on a number of occasions. In some of these cases, where the court has refused to admit the results in evidence, the principal issue has been not the scientific soundness of the tests but the authority of the court to require submission to the tests. As pointed out in the Report of the Committee on Medicolegal Blood Grouping Tests, two states, New York and Wisconsin, had at that time, 1937, passed laws specifically authorizing the courts to require submission to blood grouping tests in cases of disputed paternity and providing for the admissibility in evidence of the results of such tests. In 1939 laws were enacted in Maine, New Jersey and Ohio authorizing the courts, whenever the paternity of a child is a relevant issue in a case, to require the mother, child and reputed father to submit to blood grouping tests. All of the legislation that has been enacted to date provides that evidence of the results of such blood grouping tests will be admissible only when such tests definitely disprove the paternity of the putative father. Granting the right of a court to compel submission to blood grouping tests, either by authority of a special law as exemplified in the states named or under a more embracive statute authorizing the court to compel submission to physical examinations without specifically mentioning blood grouping tests, as was the situation in the recent District of Columbia case, there would seem to be no justification for further hesitancy on the part of the courts to accept as scientifically sound the results of blood grouping tests to the extent that they disprove the possibility of paternity.

1. Report of the Committee on Medicolegal Blood Grouping Tests, J. A. M. A. **108**: 2138 (June 19) 1937.

2. Beach v. Beach, United States Court of Appeals for the District of Columbia, No. 7559, decided June 28, 1940.

3. Frye v. United States, 54 App. D. C. 46, 293 F. 1013, 34 A. L. R. 145.

SPECIFIC SERUM IN PNEUMONIA CONTROL PROGRAM

In the recent report from the Pittsburgh Department of Public Health [1] on pneumonia treated with a specific serum from Jan. 1, 1939, to Dec. 31, 1939, the mortality was 15.7 per cent as compared to 46 per cent among cases treated by other methods. By eliminating the cases in which pneumonia occurred as a terminal infection, the mortality would have been only 8.5 per cent. A considerable variation was shown, however, in the effectiveness of serum in the different types of pneumococcic infections as well as in different age groups. Other factors likewise modified the results. It is certainly clear that specific serum treatment is effective in most types of pneumococcic pneumonia, though no light is shed by the Pittsburgh report on the comparative value of the newer chemotherapeutic agents or on the question of combined chemical and serum treatment.

1. Alexander, I. H.: Lobar Pneumonia—Pittsburgh, Pennsylvania, 1939. Department of Public Health, Pittsburgh.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

RETURN YOUR QUESTIONNAIRE!

Within ten days more than 40,000 physicians returned their questionnaires to the headquarters office of the American Medical Association supplying information to be used in the campaign for medical preparedness. An especially augmented staff is already at work checking the replies and preparing punch cards which will be used in making the selection of men for functions in preparedness and functions in any national emergency which may develop.

Every physician should return his questionnaire as soon as possible. Ultimately a punch card will be prepared for each physician in the United States, since it is necessary that every physician be represented in the file. If there is national conscription, physicians will be called as are other citizens of the United States. Great advantage to the physicians, to the Army and Navy Medical Departments, to the United States Public Health Service, and indeed to the country as a whole lies in the development of this material. With the full information once supplied, it will be possible to a considerable extent to fit every physician into work for which he is best suited.

On July 19 the Committee on Medical Preparedness met in the headquarters office of the American Medical Association with representatives of the United States Army and Navy and Public Health Service. Plans were discussed for utilization of medical personnel. There begin to be indications of the many needs which must be filled in the future. Tremendous expansion of industries associated with the manufacture of munitions and military supplies will require numbers of industrial hygienists, physicians and surgeons far beyond the number now available. Examination of many thousands of men associated with the setting up of recruiting centers, training forces and for similar objectives will again require the services not only of physicians capable of conducting routine examinations but of specialists in every medical field. Particularly important are pathologists, clinical pathologists, roentgenologists and experts in the field of cardiology, tuberculosis, and nervous and mental diseases. Finally, it is absolutely necessary to assure continuity of medical service for the civilian population.

Arrangements were made to utilize state and county societies in the extension of this work. If a physician fails to return his questionnaire, it will become necessary to ask his colleagues and his state and county medical society to be of service in determining why the physician failed to cooperate and to insure the eventual return of the information.

At a time when the nation may need the service of every patriotic citizen, the physician owes this obligation to the country and to himself. In a few instances cards and notes have been received from physicians indicating that their sympathies do not lie primarily with the needs of the country. It would be unfortunate indeed if any considerable number of physicians adopted such a point of view. The more promptly the questionnaires are returned, the greater will be the possibility of eventual action. The more accurately the information is supplied the more rapidly will it be codified. It is not only the medical profession that is on trial in this instance but democracy itself.

THE NATIONAL RESEARCH COUNCIL COMMITTEE ON CHEMOTHERAPY

ORIGIN AND OBJECTS

At the meeting of the Division of Chemistry and Chemical Technology of the National Research Council in Washington, D. C., in April 1939, the opinion was expressed that research work should be stimulated in the field of quinine substitutes and synthetic antimalarials.

While quinine, plasmoquine, atebrine and a few other drugs have been useful, there is, in the judgment of the medical profession, great need for something better. The present remedies leave much to be desired from a therapeutic point of view and the price is higher than many can afford to pay. Further, so far as quinine itself is concerned, the world is practically dependent for its supply on Java and the Kina Bureau (its selling agent) and might be cut off from this supply or perhaps compelled to pay exorbitant prices, if Java should be seized by some other nation. The trend is therefore toward synthetics as the direction which holds out the best promise of new and useful antimalarials.

Contrary to popular belief, malaria is still one of humanity's major scourges. India, with a population of some 320,000,000, has a yearly average of from 70 to 80 million sufferers, and President Fosdick of the Rockefeller Foundation, in his recent annual report, has called attention to the threatening situation in South America. In certain tropical countries the incidence of this disease is 100 per cent. Throughout the world it is stated to be the direct cause of approximately a million deaths annually.

Dr. Herbert R. Moody, chairman of the division, was duly empowered to appoint a temporary committee to survey the field of malaria and antimalarials and to report back to the division whether or not it would be advisable to designate a regular standing committee of the division to study, in cooperation with the division of medical sciences, the whole problem of the chemistry and synthesis of antimalarials.

The temporary committee appointed by Dr. Moody, from the division of chemistry and chemical technology, consisted of Dr. Leonard H. Cretcher, assistant director of the Mellon Institute of Industrial Research, Pittsburgh; Dr. Lyndon F. Small, head chemist of the National Institute of Health, U. S. Public Health Service, Washington, D. C., and Marston T. Bogert, emeritus professor of organic chemistry in residence, Columbia University, New York, as chairman.

Later, on the nomination of Dr. Esmond R. Long, chairman of the National Research Council division of medical sciences, the following members for that division were added to the temporary committee: Dr. Lowell T. Coggeshall, International Health Division, Rockefeller Foundation, New York, and Dr. Torald H. Sollmann, dean, Western Reserve University School of Medicine, Cleveland.

The completed committee thus consisted of the following chemical and medical representatives: Lowell T. Coggeshall, Leonard H. Cretcher, Lyndon F. Small, Torald H. Sollmann and Marston T. Bogert, chairman.

As a result of this preliminary survey, the temporary committee reported unanimously that, in its judgment, a regular standing committee of the division of chemistry and chemical technology should be constituted by the National Research

Council, to concern itself not solely with antimalarials, but whose function should be chemistry in the service of medicine and its title Committee on Chemotherapy, with antimalarials as its first assignment.

This broadening of the field to be covered by the committee will not reduce in any way its usefulness in an attack on the malaria problem but will permit it to offer its services in attempts to combat other diseases as well, particularly in those cases in which acute emergencies may arise and our help be welcome. Even in the investigation of antimalarials, other diseases are concerned, for example, the possible use of cinchona alkaloids or their derivatives in the treatment of pneumonia, a problem which has been under investigation by Dr. L. H. Cretcher at the Mellon Institute for a number of years.

At the meeting of the division of chemistry and chemical technology, National Research Council, Nov. 18, 1939, in Washington, D. C., the report of the temporary committee was presented and adopted and the committee was discharged. The division then recommended that the same personnel be appointed as one of its regular standing committees, to be known as its Committee on Chemotherapy. This recommendation of the division was subsequently approved by the National Research Council, and Surgeon General Thomas Parran Jr. of the U. S. Public Health Service gave his prompt consent to the service of Dr. Small on the committee.

The Academy of Tropical Medicine, the American Society of Tropical Medicine and the National Malaria Committee met at Memphis, Tenn., Nov. 21-24, 1939, and unanimously endorsed the program of the committee. The council of the American Academy of Tropical Medicine also expressed its cordial approval of the selection of Dr. L. T. Coggeshall as a member of the committee.

The Symposium on Malaria, May 29-30, 1940, in Atlanta, Ga., called by Surgeon General Parran, for the purpose of a preliminary discussion of the malaria situation in our country; with special emphasis on chemotherapy, was attended by Drs. Coggeshall and Small of the committee.

Section N of the American Association for the Advancement of Science, at its Philadelphia Meeting, Dec. 27, 1940, to Jan. 2, 1941, will hold a symposium on the human malarias, in which members of the committee will participate. The proceedings of this symposium when published will constitute an important review of present knowledge of this disease.

The objects of the committee include:

1. Chemistry in the service of medicine, with special emphasis on the discovery of new and useful synthetic drugs.

2. To bring about a closer cooperation between chemists and pharmacologists interested in the same field. It often happens that an organic chemist synthesizes a new compound of therapeutic possibilities but does not know to whom to turn to have it tested. Similarly, a pharmacologist discovers that a certain chemical exhibits hitherto unsuspected physiologic effects but has no information as to which organic chemists could help him in the preparation of the compound and its more promising derivatives.

3. To help in this direction, the committee should function as a general clearing house for the collection and classification of information as to the chemists, manufacturers, pharmacologists and others in the United States who are now at work in this field, the special lines of investigation they are following, and any other pertinent data. With this information in hand, and that accumulated last summer by the survey of research resources of educational institutions, in men and material, now classified and on file in the offices of the division of chemistry and chemical technology of the National Research Council in Washington, we should be able more intelligently to allocate and evaluate the various research problems to be investigated. In this way we can also be of some assistance in reducing the amount of unintentional duplication and overlapping in research work and suggest important problems for investigation where the need seems clearly indicated.

4. Not to undertake too ambitious a program at the outset, since the field of chemotherapy is a vast one. For the reasons explained in the foregoing pages, malaria has been selected as the first disease to be attacked.

5. To prepare a compact semipopular presentation of the malaria situation throughout the world, particularly in our own land, including a summary of what is going on here and how it is retarded and handicapped by lack of funds, for the purpose of enlisting public appreciation and support.

6. To secure funds from interested individuals, institutions, foundations, firms and others for the support of the work of the committee, the establishment of research fellowships and such other activities as will advance and expedite the achievement of the results sought.

Such a survey is now being conducted to ascertain what investigations are under way or planned for the synthesis of new and useful antimalarials, to compile a list of individuals and firms interested in this field, just what they are doing and (as far as may be possible) in what other directions they are arranging to expand.

Simultaneously, bibliographies, reviews and digests of the literature covering various aspects of the problem are being compiled, but all this work can progress but slowly under existing limitations, and speed is urgently needed; for the medical profession confidently predicts a malaria peak this year or next.

Those individuals, organizations, institutions and manufacturers who are willing to cooperate by supplying the information suggested in the foregoing pages are requested to communicate with the chairman of the committee, whose address until September 20 will be Belgrade Lakes, Maine; after that, Havemeyer Hall, Columbia University, New York.

As this committee has been for some time in touch with many others interested in antimalarials both in this and in other countries and has accumulated considerable information of value, it seems to us wise to publish this statement, in order that confusion and duplication of effort may be avoided and national preparedness advanced more speedily, for we have been informed that other committees and groups have been or are about to be organized to cover much the same field, evidently unaware of the existence of our committee and its activities.

LOWELL T. COGGESHALL.
LEONARD H. CRETCHER.
LYNDON F. SMALL.
TORALD H. SOLLMANN.
MARSTON T. BOGERT, Chairman.

CATASTROPHE UNIT

The organization of a "catastrophe unit" of doctors and nurses on the staff of Queens General Hospital, to function instantaneously in the event of a major disaster in the borough of Queens, similar to the unit on duty at Bellevue Hospital, which has already responded in four disasters of major proportions, was announced recently by Dr. S. S. Goldwater, Commissioner of Hospitals. Another unit, similar to the Bellevue emergency unit, is already on duty at Kings County Hospital, and a fourth unit is in the process of organization at Morrisania Hospital in the Bronx.

The Bellevue emergency unit, which consists of thirteen doctors and fifteen nurses, has been called out four times, the first for an explosion on Twenty-Third Street, the second for service to the battered refugees on the S. S. *Harding*, the third for a theater on One Hundred and Twenty-Fifth Street, the ceiling of which fell down, and the fourth for the recent accident at Grand Central Station. The Kings County unit has not yet been called out.

At Queens the emergency organization will consist of two alternating three squad units with four doctors and four nurses to each squad. Two of the three squads are on active call at all times, while one squad is kept in reserve.

Transportation facilities consist of a specially fitted truck supplemented by the hospital ambulances.

COMMITTEE ON MEDICAL PREPAREDNESS

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* Deceased.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Meeting at Centerville.—The northwestern division of the Medical Association of the State of Alabama held a meeting at Centerville, July 25. The speakers were Drs. Jesse P. Chapman, Selma, on "Principles Underlying the Treatment of Anemia"; Harvey B. Searcy, Tuscaloosa, "Conjunctivitis"; Neal L. Andrews, Birmingham, "Symptoms of Anorectal Disease"; James C. Gladney, Jasper, "Diagnosis and Treatment of Coronary Occlusion," and Joseph D. Wilson, Birmingham, "Surgical Management of Goiter."

ARKANSAS

Society News.—A symposium on heart disease was presented at a meeting of the Benton County Medical Society, Pea Ridge, June 13, by Drs. Charles T. Chamberlain, Ralph E. Crigler and William O. Arnold, Fort Smith.——Dr. Silas C. Fulmer, Little Rock, discussed nephritis at a meeting of the Pulaski County Medical Society, Little Rock, June 17.——Dr. P. Leo Hathcock, Fayetteville, addressed the Sebastian County Medical Society, June 11, on "Aleukemic Leukemia."

CALIFORNIA

New Student Health Service Building.—Funds have been appropriated by the regents to construct a $300,000 student health service building for the Los Angeles campus of the University of California. The plans provide a complete health service for the Los Angeles students exclusive of hospitalization. The regents increased the incidental fee on the Los Angeles campus from $23 to $25 for the added service. At present, the limited health service available to a student body of about 8,500 is crowded into cramped quarters and operated by part time employees. On the basis of experience on the Berkeley campus, it is estimated that the health service would require a floor area of about 23,500 square feet.

Society News.—A symposium on urology was presented before the Alameda County Medical Association in Oakland, June 17, by Drs. Arthur E. Dart, Herbert Stewart Kimball, Bean M. Palmer, George G. Reinle, Albert M. Meads and Leon I. Oppenheimer.——Mr. Milton H. Silverberg, Los Angeles, referee, state industrial accident commission, discussed "The Doctor and Industrial Medicine and Surgery" before the San Diego County Medical Society, June 11.

Institute on Psychiatric Education.—The first regional institute on postgraduate psychiatric education of the American Psychiatric Association was held, June 17-29, at Agnew State Hospital, Agnew. These institutes will be held throughout the country, sponsored by the committee on psychiatry in medical education, of which Dr. Franklin G. Ebaugh, Denver, is the chairman. Participating in the institute at Agnew State Hospital were, among others:

Dr. Charles A. Rymer, Denver, assistant director of the Colorado Psychopathic Hospital.

Dr. S. Spafford Ackerly, professor of psychiatry, University of Louisville School of Medicine, Louisville, Ky.

Dr. Wendell S. Muncie, associate professor of psychiatry, Johns Hopkins University School of Medicine, Baltimore.

Dr. Walter L. Treadway, assistant surgeon general, U. S. Public Health Service, now stationed at the University of California Medical School, San Francisco.

Dr. Jacob Kasanin, chief of psychiatric service, Mount Zion Hospital, San Francisco.

FLORIDA

New Health Units.—A public health unit has been created in Dade County with Dr. Turner Elam Cato, Charleston, W. Va., for many years health officer of Kanawha County, in charge. Headquarters for the new unit will be in Miami. New full time departments are also being planned for Hamilton and Nassau counties. This will bring the total number of counties served by accredited local health departments to twenty-one, newspapers reported.

Special Society Elections.—Dr. John W. Alsobrook, Plant City, was named president-elect of the Florida Railway Surgeons Association at its annual meeting in Tampa recently, and Dr. Leland F. Carlton, Tampa, was installed as president. Other officers include Drs. Zannie Brantley, Grandin, vice president, and Walter C. Page, Cocoa, secretary-treasurer.——Dr. Joseph H. Lucinian, Miami, was elected president of the Florida Radiological Society recently to succeed Dr. Harry B. McEuen, Jacksonville; Dr. John N. Moore, Ocala, vice president, and Dr. Elliott M. Hendricks, Fort Lauderdale, secretary.——Dr. Louie M. Limbaugh, Jacksonville, was elected president of the Florida Internists Society to succeed Dr. William C. Blake, Tampa, at its second annual meeting in Tampa recently. Dr. Kenneth Phillips, Miami, was reelected secretary.

GEORGIA

Society News.—At a meeting of the Emory Medical Alumni Association in Atlanta, June 6, the speakers were Drs. Richard Hugh Wood on "Pitfalls in the Therapeutic Use of Sulfanilamide and Its Derivatives"; Frank K. Boland, acute intestinal obstruction, and Clarence Dixon Fowler, infantile diarrheas.——Dr. Daniel C. Elkin, Atlanta, read a paper on "Aneurysm of the Abdominal Aorta" before the Fulton County Medical Society, Atlanta, June 20.

Hardman Cup Awarded.—Dr. William Howard Hailey, president-elect, Fulton County Medical Society, and Dr. Hugh E. Hailey, Atlanta, jointly received the L. G. Hardman Loving Cup at the annual meeting of the Medical Association of Georgia in Savannah recently for their research on "Familial Benign Chronic Pemphigus." Their work also brought them the L. C. Fischer Prize for the most original research presented before the Fulton County Medical Society in 1931. The Hardman Cup was provided by Dr. Lamartine G. Hardman, late ex-governor of Georgia, for the most original research work presented by a member of the Medical Association of Georgia in the field of public health, medicine or surgery.

ILLINOIS

Committee on Archives.—The Illinois State Medical Society has created a permanent committee on archives to collect pictures and all possible data concerning the early physicians in every county of the state. This action is the result of a photographic display at the recent state medical meeting of about 1,500 pioneer physicians of Illinois together with short sketches showing some of the highlights of their practice. The exhibit was under the supervision of Dr. Carl E. Black, Jacksonville, who has been interested in such a collection for more than fifty years.

The Fifty Year Club.—Dr. Andy Hall, Mount Vernon, was made a member of the Fifty Year Club of the Illinois State Medical Society at a special meeting of the Jefferson-Hamilton County Medical Society in Mount Vernon, June 16. Dr. Hall has been a member of the council of the state society for many years and for four years was director of the state department of public health. Since its organization about three years ago, he has been chairman of a council committee sponsoring the Fifty Year Club. About 240 physicians have been admitted to membership in the club.

IOWA

Promotions at the University.—Dr. Erwin G. Gross, who has been acting head of the department of pharmacology at the State University of Iowa College of Medicine since the death of Dr. Oscar H. Plant last October, has been made head of the department. Walter R. Ingram, Ph.D., has been made professor and head of the department of anatomy, neuroanatomy, histology and embryology, succeeding Dr. Ewen M. MacEwen, who has also been dean of the college since 1935. Dr. MacEwen will continue as professor in the department. Dr. Rubin Flocks was promoted from assistant to associate professor of urology, and Dr. Irving H. Borts to assistant professor of hygiene and preventive medicine.

KENTUCKY

Inter-County Meeting.—The Lawrence County Medical Society recently sponsored an inter-county meeting in Louisa, to which physicians from Eastern Kentucky and adjoining counties in Ohio and West Virginia were invited. Among the speakers were Drs. John W. Scott, Lexington, on "Psychoneuroses as Seen by the General Practitioner"; Irvin Abell Jr., Louisville, "Tumors of the Breast"; Elmer L. Henderson, Louisville, "Tetanus," and Arthur T. McCormack, Louisville, secretary, Kentucky State Medical Association, "Medicine Today." Dr. Robert J. Wilkinson, Huntington, W. Va., showed a motion picture on "Surgery of the Female Pelvis."

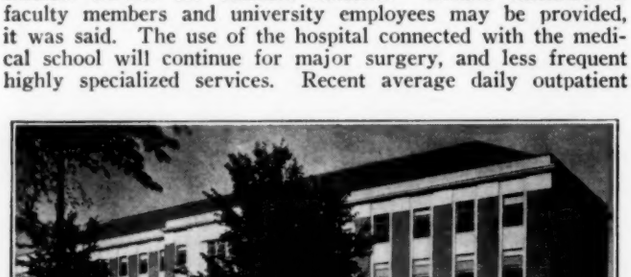
LOUISIANA

Division of Medical Extension at Tulane.—Dr. Hiram W. Kostmayer is now directing the division of medical extension at Tulane University of Louisiana School of Medicine, New Orleans, in combination with his position as director of the department of graduate medical studies.

Society News.—A special report on "Studies on the Bleeding Tendency and Vitamin K Therapy on Newborn Children" was presented before the Orleans Parish Medical Society, New Orleans, June 10, by Dr. Henry Leidenheimer Jr., among other speakers. At a recent joint meeting with the New Orleans Tuberculosis Committee the speakers were Drs. Edward L. Burns on "Pathogenesis and Pathology of Pulmonary Tuberculosis"; Emile F. Naef, "Early Diagnosis of Tuberculosis from the Standpoint of the Pediatrician," and Morell W. Miller, "Early Diagnosis of Pulmonary Tuberculosis."

MICHIGAN

New University Health Building.—The new $500,000 health service building at the University of Michigan, Ann Arbor, was recently placed in operation. Accommodations are available for sixty patients. PWA funds were used to construct the building, in which will be available a program of clinical medical service for resident students. Certain attention to faculty members and university employees may be provided, it was said. The use of the hospital connected with the medical school will continue for major surgery, and less frequent highly specialized services. Recent average daily outpatient visits amounted to 570 and annual regular session bed patient admissions have been 217 per thousand students enrolled. Operating costs of the health service total about $15 annually for each student, and these are defrayed from the regular tuition fees. Dr. Warren E. Forsythe is director of the health service.



New university health building.

MISSOURI

Officers of Clinical Society.—Dr. Cabray Wortley was recently elected president of the St. Joseph Clinical Society, succeeding Dr. Charles Greenberg. Other officers include Drs. Francis X. Hartigan and Leon Paul Forgrave, vice presidents; Harold E. Petersen, secretary.

Personal.—Edward Adelbert Doisy, Ph.D., professor and director of the department of biochemistry, St. Louis University School of Medicine, received the honorary degree of doctor of science from Washington University, St. Louis.——Dr. Arthur R. McComas, Sturgeon, was the guest of honor at a picnic near Columbia, recently, given by the Boone County Medical Society to celebrate his completion of fifty years in the practice of medicine.——Dr. Nathan K. Pope, assistant superintendent of the Missouri State School, Marshall, has been appointed superintendent of the criminal insane division of the Fulton State Hospital, Fulton, succeeding Dr. Thomas R. Frazer, who resigned several months ago.

NEBRASKA

State Medical Election.—Dr. William P. Wherry, Omaha, was named president-elect of the Nebraska State Medical Association at the recent annual meeting in Omaha and Dr. Clayton F. Andrews, Lincoln, was named president-elect. Drs. Albert A. Ashby, Fairmont, and Albert L. Cooper, Scottsbluff, were elected vice presidents. Dr. Roy B. Adams, Lincoln, is secretary. Next year's meeting will be in Lincoln, May 5-8.

NEW YORK

Personal.—The Schenectady County Medical Society honored Drs. Henry G. Hughes, Henry A. Kurth and Morris S. Lord at a meeting, June 6, on their completion of fifty years of practice. Dr. Frank Vander Bogert, program chairman for thirty years, was presented with a walking stick.——Dr. Albert D. Kaiser, Rochester, has been appointed by Governor Lehman to be a member of the temporary legislative commission to formulate a long range health program, succeeding the late Dr. Thomas P. Farmer, Syracuse.

New York City

Gifts to St. Luke's Hospital.—Announcement is made of the recent donation to St. Luke's Hospital of the following amounts: $10,000 from an anonymous friend for an endowment fund for special nursing; $2,000 from various friends to remodel the orthopedic ward; $2,000 from an anonymous donor for the ear, nose and throat department; $7,500 each from the estates of Andrew Purdy and Louise Baier to endow ward beds; $9,000 from the Henrietta T. Jones estate for care of sick nurses; $6,614.60 for general purposes from churches and friends, and various smaller amounts.

Appointments for Tuberculosis Hospital.—Senior staff members for the city's new tuberculosis unit, the Triboro Hospital, nearing completion in Queens, were announced by Dr. Sigismund S. Goldwater after selection by an advisory committee. Drs. Richard H. Bennett and H. McLeod Riggins will be directors of medicine; Henry W. Louria and Daniel A. Mulvihill, directors of surgery; Abraham Braunstein, Long Island City, visiting physician; Cranston W. Holman and Herbert C. Maier, visiting surgeons. The medical board will now be organized and will nominate additional staff members of all ranks to complete the visiting staff of about eighty members. It is expected that the hospital will be in operation by Jan. 1, 1941.

Dr. Sherman Given Borden Award.—The Borden Award for research in nutrition was awarded to Henry C. Sherman, Ph.D., Mitchill professor of chemistry, Columbia University, at the meeting of the American Home Economics Association in Cleveland, June 23-28. The award is a medal and $1,000. Dr. Sherman has been on the Columbia faculty since 1897 and has conducted research on enzymes, vitamins and the mineral elements in nutrition. He has served as president of the Society of Biological Chemists and has been honored with the Nichols Medal of the American Chemical Society and with the medal of the American Institute of Chemists. The Borden Award has previously been given to Amy L. Daniels, Ph.D., University of Iowa, Iowa City; Lydia J. Roberts, Ph.D., University of Chicago, and Icie Macy-Hoobler, Ph.D., Detroit.

OHIO

Society News.—Dr. Richard Hotz, Toledo, discussed "Differential Diagnosis of Biliary Tract Lesions" before the Academy of Medicine of Toledo and Lucas County, June 7.——Dr. Richard H. Freyberg, Ann Arbor, Mich., addressed the Mahoning County Medical Society, Youngstown, June 18, presenting "Appraisal of Some Adjuncts in the Treatment of Chronic Arthritis."

Public Health Association.—Dr. Charles A. Doan, Columbus, was reelected president of the Ohio Public Health Association at the annual meeting in Cleveland, June 5, during the annual session of the National Tuberculosis Association. Dr. Henry Kennon Dunham, Cincinnati, and Floyd A. Rowe, Cleveland, were elected vice presidents, and James E. Hagerty, Ph.D., Columbus, secretary. Dr. Herbert R. Edwards, New York, was the guest speaker on "Revitalizing the Tuberculosis Control Problem."

Physicians Honored.—Dr. George C. Jameson, Oberlin, was honored at the recent commencement of Oberlin College on the fiftieth anniversary of his graduation from the college. He was guest of honor at a dinner in recognition of his forty-six years on the faculty committee of athletics and was honorary marshal at the commencement.——Dr. John A. Riebel, Columbus, received the honorary degree of doctor of laws from Capital University, Columbus, at the June commencement.——Dr. Philip Zenner, Cincinnati, a physician for sixty-five years, was the honor guest of the Alumni Association of the University of Cincinnati College of Medicine at its annual dinner, June 6. He was formerly professor of neurology and psychiatry at the medical college and is now professor of neurology emeritus.

PENNSYLVANIA

District Meeting.—A program on diabetes featured a meeting of the Eighth Councilor District of the Medical Society of the State of Pennsylvania at Warren, June 5. The speakers were Drs. Belford C. Blaine, Pottsville; George Booth, Pittsburgh; Frank A. Evans, Pittsburgh, and Edward W. Alton Ochsner, New Orleans. Drs. Charles H. Henninger, Pittsburgh, president of the state society; Chauncey L. Palmer, Pittsburgh, chairman of the committee on public health legislation, and Walter F. Donaldson, Pittsburgh, secretary, also delivered addresses. Testimonial certificates for fifty years or more of practice were presented to Drs. Myron A. Bailey, Jamestown; Michael V. Ball, Warren; Otis S. Brown, Warren; Burg Chadwick, Smethport; Glennis E. Humphrey, Cambridge Springs; Hugh Jameson, Titusville; Andrew J. Mitchell, Sharon; Hiram B. Russell, Sheffield, and Monroe T. Smith, Warren.

Philadelphia

Personal.—Dr. John F. Sinclair has resigned as medical director of the Babies' Hospital of Philadelphia, it is reported. ——Dr. Charles L. Brown has been appointed visiting physician in the medical wards of the Philadelphia General Hospital to succeed the late Dr. David Riesman. —— Dr. Alfred N. Richards, professor of pharmacology, University of Pennsylvania School of Medicine, received the honorary degree of doctor of science at the annual commencement of Harvard University, June 20.

Laboratory for Standardization of Biological Stains Moved to Philadelphia.—The research and control laboratory of the Commission on the Standardization of Biological Stains, formerly located at the Arlington (Va.) Experimental Farm of the Bureau of Agricultural Chemistry and Engineering of the U. S. Department of Agriculture, has been moved to the Philadelphia College of Pharmacy and Science. This laboratory was established in 1920, at the suggestion of the Society of American Bacteriologists and under the auspices of the National Research Council, with a grant from the Chemical Foundation. Its work is to analyze dyestuffs to be employed for biological stains for identification and for diagnostic determinations. It also works toward improvement in existing products and the synthesis of new dyes for specific purposes. The chairman of the commission is Harold J. Conn, Ph.D., New York Agricultural Experiment Station, Geneva, N. Y. The director of the laboratory is Mrs. Anis P. Bradshaw.

RHODE ISLAND

State Medical Meeting and Election.—Dr. Frederick V. Hussey, Providence, was named president-elect of the Rhode Island Medical Society at the annual meeting in Providence in June, and Dr. Lucius C. Kingman, Providence, was installed as president. Dr. Guy W. Wells is secretary. Morning sessions were held at Providence hospitals and afternoon programs at the Rhode Island Medical Library. The speakers were:

Dr. Robert F. Loeb, New York, Adrenal Insufficiency and Its Present-Day Management.
Dr. Elliott P. Joslin, Boston, Incidence of Diabetes in Rhode Island and Other States.
Dr. Torr Wagner Harmer, Boston, Observations on Hand Surgery.
Dr. Charles P. Fitzpatrick, Howard, Some Aspects of Convulsive Disorders.
Dr. Clifton B. Leech, Providence, Luetic Heart Disease in Rhode Island.
Dr. Walter G. Phippen, Salem, Mass., Medical Service and the National Health Program.
Dr. Robert L. Maynard, Burlington, Vt., Reduction of Fractures of the Acetabulum with Penetration of the Head of the Femur into the Pelvis.

At an evening session Clarence C. Little, Sc.D., Bar Harbor, Maine, managing director of the American Society for the Control of Cancer, made an address on "Progress in Cancer Control."

SOUTH DAKOTA

State Medical Election.—Dr. Bertrand M. Hart, Onida, was chosen president-elect of the South Dakota State Medical Association at its annual meeting in Watertown in May and Dr. Oscar J. Mabee, Mitchell, was inducted into the presidency. Dr. Clarence E. Sherwood, Madison, was reelected secretary for a three year term. The 1941 session will be in Mitchell.

TENNESSEE

Regional Meetings.—Dr. George W. Crile, Cleveland, was the guest speaker at the annual session of the West Tennessee Medical and Surgical Association in Jackson, recently, on "Essential Hypertension." Among other speakers were Drs. Jefferson C. Pennington and Spencer Johnson, Nashville, on "Diagnosis and Management of Prostatic Enlargement"; Conley H. Sanford, Memphis, "The Role of Amebiasis in Chronic Digestive Disorders" and Arthur F. Cooper, Memphis, on the work of the National Physicians' Committee for the Extension of Medical Service. Dr. George W. Brasher, Jackson, was elected president.——Speakers at the semiannual meeting of the Middle Tennessee Medical Association in Spring Hill, recently, included Drs. Eugene M. Regen and Cobb Pilcher, Nashville, on "Low Backache with the Sciatic Syndrome"; James C. Kelton, Lascassas, "Chronic Mucous Colitis"; Sam C. Cowan, Nashville, "Puerperal Infection," and William R. Cate, Nashville, "Cardiac Asthma." Dr. Bernard H. Woodard, Spring Hill, was elected president.

TEXAS

Course in Obstetrics and Pediatrics.—Baylor University College of Medicine, Dallas, conducted a postgraduate course in obstetrics for general practitioners, May 20-June 15, in cooperation with the committee on postgraduate medical education of the Texas State Medical Association and the division of maternal and child welfare of the state department of health.

Special Society Elections.—Dr. Wilmer L. Allison, Fort Worth, was elected president of the Texas Neurological Society at its recent annual meeting in Dallas; Drs. William Thomas, Terrell, and Elza M. Perry, Dallas, were elected vice presidents, and Melbourne J. Cooper, San Antonio, secretary.—— Dr. Khleber H. Beall, Fort Worth, was chosen president of the Texas State Heart Association at its annual meeting in Dallas, May 13; Dr. Edwin Ghent Graves, Houston, was named vice president, and Dr. Victor E. Schulze, San Angelo, secretary-treasurer.

Veteran Physicians Honored.—The Bexar County Medical Society, San Antonio, gave a banquet recently in honor of ten members who have practiced more than fifty years. Dr. Walter G. Stuck presided and delivered an address complimenting the guests of honor, and Dr. Patrick I. Nixon spoke on "Foundation Builders." The veteran practitioners are Drs. Sigmund S. Burg, Oscar B. Manes, James P. Oldham, G. Graham Watts, Frank S. White, John H. Burleson, David Cerna and Edward F. Hertzberg, all of San Antonio; Robert E. Moss, La Grange, and Adolph Herff, Boerne.

Society News.—The Dallas Southern Clinical Society recently elected the following officers: Drs. Everett C. Fox, president; Howard K. Crutcher, vice president, and Charles H. Warren, secretary. The thirteenth annual spring clinical conference will be held at the Hotel Adolphus, March 17-20, 1941. ——Drs. Alfred L. Ridings and Max R. Woodward, Sherman, addressed the Hunt-Rockwall-Rains Counties Medical Society, June 11, in Greenville, on "Pathology of the Cervix" and "Feeding of the Sick Infant" respectively.——At a meeting of the Dallas County Medical Society, Dallas, June 27, the speakers were Drs. Hubert F. Hawkins on "Obscure Heart Disease"; Walter H. Moursund, "Heat Exhaustion of Non-industrial Origin," and Claude D. Winborn, "In Defense of Submucous Resection."

VIRGINIA

Personal.—Dr. John E. K. Flannagan, Marion, was recently appointed superintendent and medical director of the Municipal Tuberculosis Sanatorium at Roanoke.——Dr. Clyde F. Ross, Richmond, has been appointed venereal disease control officer of the city, succeeding Dr. Francis W. Upshur.

Eye and Ear Specialists Meet.—Dr. George G. Hankins, Newport News, was elected president of the Virginia Society of Ophthalmology and Otolaryngology at the recent annual meeting at Old Point Comfort. Dr. Mortimer H. Williams, Roanoke, was made vice president and Dr. Guy R. Fisher, Staunton, secretary. The guest speakers were Drs. Lyman G. Richards, Boston, on "Diagnosis and Treatment of Sinus Disease in Children" and Frank B. Walsh, Baltimore, "Ocular Signs of Thrombosis of the Dural Sinuses."

WISCONSIN

Outbreak of Poliomyelitis. — Six cases of poliomyelitis have recently been reported in Florence County. Health authorities asked that public gatherings be restricted and that children be kept at home.

Dr. Koehler Retires.—Dr. John P. Koehler, health commissioner of Milwaukee since 1925, was to retire July 1, according to the *Wisconsin Medical Journal.* Dr. Koehler graduated from the University of Nebraska and the Chicago Theological Seminary before entering Milwaukee Medical College, an immediate predecessor of Marquette University School of Medicine. He received his medical degree in 1911. After several years of practice he was appointed deputy health officer

of Milwaukee in 1918. During his administration the city has won first place in the national health conservation contest four times and second place three times.

Society News.—Drs. Walter A. Fansler, Minneapolis, and William J. Carson, Milwaukee, addressed the Barron-Washburn-Sawyer-Burnett Counties Medical Society in Rice Lake, recently, on "Diagnosis and Treatment of Anorectal Diseases" and "Surgical Infection of the Kidney" respectively.——Drs. Reuben H. Stiehm and William H. Oatway Jr., Madison, addressed the Rock County Medical Society, Janesville, recently, on "Subclinical Pulmonary Tuberculosis" and "Modern Collapse Therapy of Pulmonary Tuberculosis" respectively. Dr. Adrien H. Verbrugghen, Chicago, was the speaker, June 26, on "Treatment of Spinal Injuries."——Dr. Walter A. Brussock, Milwaukee, addressed the Washington-Ozaukee Counties Medical Society, Hartford, recently, on treatment of heart disease.

PUERTO RICO

District Meeting.—At a meeting of the Mayaguez District Medical Society at Yauco, July 7, the speakers included Drs. Ramón T. Colón, Mayaguez, "Prognostic Value of the Conversion of the Sputum"; Thomas H. D. Griffitts, senior surgeon, U. S. Public Health Service, "Protective Measures Against the Introduction of Yellow Fever"; Gabriel E. Rigau, Yauco, "Molasses and Its Use in Medicine"; Ramón M. Suarez, San Juan, "Treatment of the Asthmatic Status"; Manuel Guzman Rodriguez Jr., Mayaguez, "The Hilar Shadow in the Diagnosis of Infantile Tuberculosis." The motion picture "With These Weapons" was shown with introduction by Dr. Ernesto Quintero, San Juan, and Dr. Armando Antommattei, Yauco, reported "A Bicephalic Case."

GENERAL

Meeting of Insurance Physicians.—Dr. Albert J. Robinson, Hartford, Conn., was elected chairman of the medical section of the American Life Convention at the thirtieth annual meeting of this group in Colorado Springs, June 4-6, and Dr. Benjamin F. Byrd, Nashville, Tenn., was reelected secretary. Among the speakers were Drs. Harry E. Ungerleider, New York, on "Cardiac Arrhythmia" and Albert R. Tormey, Madison, Wis., "Osteomyelitis."

Placement Bureau for Use by Radiologists. — The American Registry of X-Ray Technicians announces the establishment of a placement bureau. The services of the bureau will be limited to physician-radiologists of approved standing and x-ray technicians who have been certified by the registry. It will operate without fees. Applicants for positions will be classified according to their added abilities as nurses, laboratory technicians or other qualifications. Physician-radiologists wishing to register a vacancy for an x-ray technician with the placement bureau may do so by writing to Alfred B. Greene, R.T., executive secretary, American Registry of X-ray Technicians, Oak Terrace, Minn.

Cancer Institute to Publish Journal. — The National Cancer Institute, Bethesda, Md., announces the forthcoming publication of the *Journal of the National Cancer Institute*, to be issued bimonthly. The journal will contain articles by members of the staff of the institute, which is a unit of the National Institute of Health, U. S. Public Health Service. The subscription price will be $3 a year in the United States. The journal will be distributed free to a limited number of medical schools, to workers in the fields of cancer research, to research institutes interested in cancer, to a limited number of surgeons as well as to certain government depositories and to journals making suitable exchanges.

Poliomyelitis Increased in 1939.—A sharp increase in the number of cases of poliomyelitis was reported in 1939 over the total recorded in 1938, according to figures released by the U. S. Public Health Service. There were 7,272 cases in 1939 as compared with 1,705 cases in 1938. The latter was considered a year of unusually low incidence. In 1939 the distribution of the disease was characterized by a number of localized outbreaks in various sections of the country in addition to a fairly widespread occurrence in the mountain states. The case rate was highest in New Mexico, South Carolina, Arizona and Minnesota, followed by Michigan, Utah and California. The most extensive area included a group of counties in Arizona, Utah, New Mexico, Colorado and northwestern Texas. The second largest area extended across central Minnesota and included a few counties in northeastern South Dakota. Smaller groups of counties in which the incidence was high were located in Michigan, New York, South Carolina, Kentucky, Iowa and south central California. Two adjoining counties in New Jersey and Philadelphia comprised a very small area in which the incidence of poliomyelitis was moderately high.

Changes in Status of Licensure. — The Massachusetts Board of Registration in Medicine reports the following action taken at a meeting June 6:

Dr. Joseph D. Beauparlant, Fall River, license revoked on account of conviction of abortion.

The state board of health of Missouri recently reported the following actions:

Dr. Charles M. Yaley, St. Louis, license revoked, June 6, for unprofessional and dishonorable conduct.

Dr. James Monroe Brotherton, Kennett, license revoked in April for unprofessional and dishonorable conduct.

The Public Health Council of West Virginia reports the following action:

License of Dr. Paul Foreman Weist, formerly of Charles Town, revoked July 1 on the grounds of conviction of a felony under the Maryland Uniform Narcotic Act while he was under probation to the Public Health Council following a previous conviction under the federal narcotic act.

Assistant Managing Director Appointed for Cancer Society. — Dr. James Samuel Binkley, New York, has been appointed assistant managing director of the American Society for the Control of Cancer, effective June 1. He will divide his time between the society and his work on the staff of Memorial Hospital for the Treatment of Cancer and Allied Diseases. Dr. Binkley is a native of Oklahoma and graduated from Harvard Medical School, Boston, in 1932. He engaged in private practice in Oklahoma City and went to Memorial Hospital in 1936 as assistant resident surgeon. During the past year he has been resident surgeon. He spent February and March giving a series of postgraduate lectures in forty towns and cities in Oklahoma under the auspices of the state medical association, the state department of health and the Women's Field Army of the American Society for the Control of Cancer.

Young Physician Disappears. — Dr. Runyon H. Irvin, Mount Vernon, Ill., disappeared from his home June 2 and has not been heard from since. His mother, Mrs. Grant Irvin, requests that any information concerning him be telephoned collect to her at Mount Vernon, telephone number 1015, or to Dr. Todd P. Ward, telephone 59, Mount Vernon. She asks also that if he is located he be advised to telephone her if he needs funds. Dr. Irvin had suffered a nervous breakdown during the past year but was thought to be improved. He is 32 years old, 5 feet 11 inches tall, weighs 160 pounds, has a fair complexion, light hair and blue eyes. He was wearing a grayish blue winter suit, a white straw sailor hat and black shoes, size 11.

Special Society Elections.—Dr. Paul P. McCain, Sanatorium, N. C., was elected president of the National Tuberculosis Association at the annual meeting in Cleveland, June 3-6. Drs. James Burns Amberson Jr., New York, and Grover C. Bellinger, Salem, Ore., were elected vice presidents and Dr. Charles J. Hatfield, Philadelphia, was reelected secretary. President Roosevelt and Surgeon General Thomas Parran of the U. S. Public Health Service were made honorary vice presidents.——Dr. Clement J. DeBere, Chicago, was elected president of the American Proctologic Society at the annual meeting in Richmond, Va., June 9-11. Dr. John J. Corbett, Detroit, was elected vice president and Dr. William H. Daniel, Los Angeles, secretary.——Dr. Fraser B. Gurd, Montreal, was elected president of the American Association of Thoracic Surgery at its annual meeting in Cleveland in June. Dr. Edward D. Churchill, Boston, was elected vice president and Dr. Richard H. Meade Jr., Philadelphia, reelected secretary. ——Dr. Harold G. Trimble, Oakland, Calif., was named president-elect of the American Trudeau Society at its annual meeting in Cleveland, June 3, and Dr. Lewis J. Moorman,

Oklahoma City, became president. Dr. Victor F. Cullen, State Sanatorium, Md., was elected vice president and Dr. Benjamin L. Brock, Waverly Hills, Ky., secretary.——Dr. James A. Babbitt, Philadelphia, was named president-elect of the American Laryngological, Rhinological and Otological Society at the annual meeting in New York, June 8, and Dr. John MacKenzie Brown, Los Angeles, became president. Vice presidents elected were Drs. Nelson S. Weinberger, Sayre, Pa.; William G. Kennon, Nashville, Tenn.; Walter H. Theobald, Chicago, and Robert C. Martin, San Francisco. Dr. Carlton S. Nash, Rochester, N. Y., is secretary. The 1941 convention will be in Los Angeles.——Dr. Louis Faugeres Bishop Jr., New York, was elected president of the American Therapeutic Society at the annual meeting in New York in June. Dr. Oscar B. Hunter, Washington, D. C., is secretary.——Dr. Bernard J. Alpers, Philadelphia, was elected president of the American Association of Neuropathologists at the annual meeting in Rye, N. Y., June 6; Dr. Roy R. Grinker, Chicago, was elected vice president, and Dr. Armando Ferraro, New York, secretary.

LATIN AMERICA

Congress on Tuberculosis.—The Fifth Pan American Congress on Tuberculosis will be held under the auspices of the Latin American Union of Tuberculosis Societies in Buenos Aires, October 13-15, and in Cordoba, October 16-17. Official subjects for discussion will be the tuberculosis index of South American countries, heredity and contagion in tuberculosis and the lungs in extrathoracic forms of tuberculosis. Each member nation of the union will have an official speaker on each subject. An attendance fee of 10 pesos, Argentine currency, has been set for members of the congress and a fee of 5 pesos for members of their families, allowing them to participate in official activities but not in the deliberations of the congress. Fees may be sent to and other information may be obtained from the chairman, Dr. Gumersindo Sayago, 9 de Julio, 691, Cordoba, Argentina.

CORRECTION

Dr. Jones.—In THE JOURNAL, June 1, page 2230, in an announcement of the annual meeting of the American Neisserian Society, it was stated that a paper on "Correlating the Micropathology and the Clinical Findings in Gonorrhea" would be given by Dr. William Ray Jones, Minneapolis. This should have been Dr. Walter Raymond Jones, Seattle.

Government Services

New Director of Malaria Research Laboratory

Dr. Hiram J. Bush, U. S. Public Health Service, has been named director of the Henry R. Carter Memorial Laboratory for Malarial Research, Savannah. He succeeds Dr. Thomas H. D. Griffitts, who was transferred to Puerto Rico several months ago, as chief quarantine officer. Dr. Charles M. McGill has been acting director of the laboratory since Dr. Griffitts' departure. Dr. Bush graduated at the University of Pittsburgh School of Medicine in 1927.

New District Health Unit in New Orleans

The U. S. Public Health Service has established a permanent health district unit with headquarters in New Orleans, newspapers reported recently. The unit will supervise public health service work in Texas, Louisiana, Florida, Alabama, Georgia, Mississippi and Tennessee. Dr. Charles L. Williams, assistant surgeon general, U. S. Public Health Service, will be in charge of the unit, which was expected to begin operations July 1.

New Marine Hospital at Boston

A new building for the U. S. Marine Hospital, U. S. Public Health Service, Boston, was dedicated June 6, with Paul V. McNutt, Federal Security Administrator, as the principal speaker. Drs. Thomas Parran, Surgeon General, and Sanders L. Christian, chief of the division of marine hospitals and relief, U. S. Public Health Service, were other speakers at the ceremonies. At a luncheon in connection with the exercises, Dr. Roger I. Lee, Boston, was the speaker. The new 360 bed hospital is on Warren Street near Commonwealth Avenue.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 29, 1940.

Bomb Hospital Ships

In reply to a question in the House of Commons, the government stated that since the outbreak of war nine hospital ships have been bombed, shelled or machine gunned—two of them on more than one occasion—despite the vessel's distinctive and unmistakable markings and in contempt of the lives of the wounded and of the doctors and nurses attending to them. The hospital ship *Atlantis* alone was bombed no less than five times in Norwegian waters. The only sinking was that of the hospital carrier *Paris*, June 2, which succumbed to three separate waves by bomber aircraft. The hospital carrier *Brighton* was holed and run aground; the hospital carrier *Maid of Kent* was set on fire. In his speech dealing with the embarkation of the allied troops from Dunkirk, Mr. Churchill stated that the hospital ships which brought off many thousands of British and French wounded, though plainly marked, were a special target for enemy bombs. The *Paris*, which had no wounded on board at the time of the bombing, had to be abandoned after the dropping of twelve bombs. An hour later the aircraft returned and machine-gunned the army medical corps and the nurses who were taking to the boats. A bomb hit the davit of a boat carrying six nurses, throwing them into the sea. They were pulled out with ropes, but one was badly wounded in the arm. It was suggested in Parliament that as the Red Cross is not respected and even seems to attract attack, its use should be discontinued, but a decision on this point has not been made. It has also been suggested that hospital ships should be armed or convoyed.

Americans Give Ambulances

As a gesture in the present emergency, Americans in Britain are to equip and maintain a large ambulance service, which will be known as the American Ambulance, Great Britain. It will number at least 200 well equipped ambulances and mobile first aid units. The drive to raise funds was launched not long ago by well known members of the American colony in London. Funds will be raised entirely from American individuals and social and commercial organizations here and in the United States. A start was given when the American ambassador, Mr. Joseph Kennedy, made in the name of his wife a contribution sufficient to supply and maintain a completely equipped ambulance for one year. Mr. Kennedy's gesture has been followed by the gift of six eight cylinder saloon cars from Packard Cars. Four Chrysler and two eight cylinder Dodge cars have been contributed by Chrysler Motors Ltd.

Departure of Sir Aldo Castellani

On the entry of Italy into the war the large Italian population in this country was interned. But a party of Italians, amounting to 700, consisting of consuls and others, have been shipped to Italy with the Italian ambassador. Among these was Sir Aldo Castellani, the authority on tropical medicine. An Italian by birth, he settled in London, where he attained high position, becoming a fellow of the Royal College of Physicians and director of mycology and lecturer at the London School of Tropical Medicine. He received the decoration of K.C.M.G. from the British government and was editor of the *Journal of Tropical Medicine*. He was the principal medical officer in the Italian expedition against Abyssinia. At one time he held the chair of tropical medicine at the Louisiana State University, New Orleans.

Italy as a Source of Drugs

The entrance of Italy into the war has removed a source of drug supply, particularly of essential oils. Great quantities of Sicilian lemon, orange, bergamot and mandarin oils are shipped from Messina to the world's trading centers, but fortunately these articles are produced on a large scale in other countries. In recent years Italian shippers have met with increasing competition, notably from the California producers of lemon oil and West African producers of orange oil. California is now sending to this country a cold pressed lemon oil (as distinguished from the distilled oil) which compares favorably in taste and aroma with the celebrated Sicilian hand pressed oil and is sold at half the price. French Guinea began to export orange oil in recent years and has made remarkable progress. At one time Italy possessed almost a monopoly of citric acid, but this trade is now of little importance because of the large production of synthetic citric acid. The stoppage of exports from Barri of Italian olive oil is not of great moment, as vegetable oils such as peanut, sesame and cottonseed oil are equally suitable for edible and for medicinal uses. Squill and manna come so much from Italy that there is a shortage, but the latter is not now much used in medicine. Liquorice juice and sulfur come largely from Italy but there are important other sources.

The British Postgraduate Medical School

The dean's annual report of the British Postgraduate Medical School states that the year has been one of steady progress in the development of postgraduate education. The most noteworthy advance was provision of an organized course for the diploma in clinical pathology. This has been available for the last eight years, but up to 1937 only five candidates had satisfied the examiners. This was mainly due to difficulty in obtaining instruction covering the whole field. Applications for the course were received from India and the dominions as well as from home. Only half the applications for admission could be accepted. A testimony to the standing of the school is that the American Board of Internal Medicine has recognized it as one of the foreign medical schools where students may spend the first three years in study.

BUENOS AIRES

(From Our Regular Correspondent)

June 7, 1940.

Number of Physicians in Argentina

According to the report of a special commission, there are 11,244 physicians in Argentina, one for every 1,485 inhabitants. Of these, 5,077 live in Buenos Aires. This leaves some parts of the country scantily provided. In several northern provinces, for example in Santiago del Estero and in San Luis, one physician is found to 5,569 and 5,645 inhabitants, respectively. In the province of Tucumán the proportion is that of one physician to 3,048 inhabitants, but of the 164 physicians 120 reside in the capital of the province (125,000 inhabitants) leaving forty-four physicians for the rest of the province (375,000 inhabitants), which means a ratio of one physician to 8,522 inhabitants. In the city of Buenos Aires the ratio is one physician to 625 inhabitants.

Transporting Patients by Airplane

Dr. Mariano R. Castex, professor of internal medicine in Buenos Aires, with the collaboration of Dr. Capdehourat and Dr. Orosco, investigated the effect of the transportation by air on persons with cardiac and pulmonary diseases. They utilized the data obtained by the scientific mission sent by Argentina to the Bolivian plateaus. Low barometric pressure, they found, provokes a syndrome of hypoxemia and hypocapnia. Gas alkalosis induced by increased excretion of carbon dioxide favors arterial oxygenation by influencing the hydrogen ion concentration toward the alkaline side. These modifications together with the increase of erythrocytes and hemoglobin constitute the chief factors in adjustment to the altitude. Careful analysis of the effect of altitude on the heart, lungs and respiratory apparatus of normal as well as ill persons has led Castex and his associates to the conclusion that of persons with cardiac and circulatory disorders only those with myocardia can be safely transported through the air, under certain conditions. In cases of respiratory disorders only those affected with bronchial or chronic pleural disorders of a nonexudative nature can be safely flown through the air. In general, the investigations showed that the effects on persons who fly at a high altitude are analogous to those on persons who live at high altitudes. The only difference consists in the duration of the effect.

Congress for Social Welfare

The first meeting of the National Congress of Sociology, Social Welfare and Medical Needs of Workers is to meet in Córdoba October 14-19. The section on legislative proposals will deal with the relation between cardiopathies and occupational illnesses, carcinoma as an occupational illness, tuberculosis, agricultural labor, revision of the law governing accidents during work, and occupational diseases. The section on social welfare will deal with social security, the constitution of workers and the employment of those under age. The section on medical needs of workers will discuss cancer prevention, pneumoconiosis, neuroses due to occupational work and whether carcinoma, tuberculosis and cardiopathies are to be regarded as occupational illnesses.

Control of Infectious Diseases

Recently the Argentine society of epidemiology and control of infectious diseases (Sociedad argentina de epidemología y lucha contra las enfermedades infecciosas) was founded in Buenos Aires. Its purpose is to promote research, develop training courses and establish close contact with similar societies abroad. It will work in cooperation with the José Penna Institute for Infectious Diseases of the medical faculty of Buenos Aires. Professor Carlos Fonso Gandolfo was elected president. The institute has been granted permission to sell patriotic stamps to be released annually May 25, the Uruguayan memorial day, to raise funds for fighting infectious diseases.

Joint Sessions of Pediatric Societies

The tenth session of the pediatric society was held jointly with the Uruguayan pediatric society to commemorate the twenty-fifth anniversary of the latter society. Representatives from the United States, Argentina, Chile, Paraguay and Ecuador participated. The Instituto internacional Americano de protección a la infancia alsó took part in the celebration. The subjects discussed included electrocardiography in pediatrics and the etiology of infections in children's diarrhea. Technical commissions are to be sent to Bolivia and Paraguay to study the morbidity and mortality in children and to work out a plan for child protection. Extensive investigations are also to be undertaken relating to the nutrition of children and mothers in Latin America.

Obstetric Facilities in Venezuela

Oropeza recently reported that in 1936, on the average, 469 births took place every month in the city of Caracas, 170 in public and private institutions, 150 at home under the care of physicians and the remaining 149 managed by midwives mostly without special training. Since 1936 an obstetric clinic has been constructed in which about 263 deliveries take place every month out of 565 monthly births now reported. Caracas, the capital of the nation, is the only city which possesses a well organized medical organization of a public nature. In the remaining cities of the country almost all children are delivered by untrained

midwives. In spite of these conditions, one of the significant causes of children's mortality, namely tetanus, has been reduced from 2,324 in 1922 to 871 in 1932 and to 225 in 1938. The division for mothers and children of the department of health and social aid, in the bulletin of which Oropeza's article appeared, has issued directions governing obstetric aid, the most important and dangerous infant diseases and proper nutrition. In the state budget for last year 1,200,000 bolivares (about $240,000) was allocated for child aid. This sum is exclusive of subsidies to other institutions.

Child Welfare

The bureau of maternal and child welfare (dirección de maternidad y infancia) has been gathering information for two years in numerous private institutions for preschool children. It was found that a large number of children between the ages of 2 and 6 years showed defects or disease conditions. Dental caries and disorders affecting the nose, throat and ears predominated together with parasitism in certain centers. Extensive measures are being taken to combat these diseases by educating the families involved, especially in the poorer sections, and by following up the development of preschool children who have been examined.

Coming Meetings

The eighth congress of the Pan American Medical Association will meet in 1941 in Buenos Aires under the presidency of Prof. José Arce, professor of surgery. It will be organized in twenty-four sections.

The fifth Pan American Conference of National Directors of Public Health is to meet in 1942 in Rio de Janeiro.

An Argentine branch of the Inter-American Society of Microbiology has been organized in Buenos Aires. The society was founded last year in New York in connection with the third International Congress of Microbiology. Prof. Alfredo Sordelli, director of the bacteriologic institute of the national health department in Buenos Aires, is president. Dr. F. Duran Reynals of Yale University is general secretary of the parent association. Further branches are planned for Uruguay, Peru, Chile and Brazil. The Argentine branch is housed in the bacteriologic institute.

The first National Congress of Pediatrics will be held in Buenos Aires October 7-11. The official subjects are growth and physical development, mental development, rickets and the prevention of tuberculosis and syphilis.

Health Propaganda

The national department of public health in Buenos Aires has announced the functions to be exercised by its division on promotion of health and sanitation. It is to educate the public on disease prevention, accidents, drug addiction, poisoning, physical and mental hygiene, and nutrition. A radio program has been arranged furnishing two broadcasts a week over a government station.

Personals

Prof. Angel H. Roffo in Buenos Aires has been nominated *honoris causa* as associate professor of the Universidad Mayor de San Andrés in La Paz, Bolivia.

Prof. Juan Ramón Beltrán, professor of the history of medicine in Buenos Aires, has been appointed an honorary member of the society for the history of medicine in New York.

Prof. B. A. Houssay, professor of physiology in Buenos Aires, has been appointed a foreign member of the U. S. National Academy of Sciences.

Prof. Ignacio Imaz, on reaching the retiring age, has resigned. Dr. Mario Soto, associate professor of pharmacology and therapy on the medical faculty of Buenos Aires, has been named to succeed him.

Marriages

JAROUD BENONIA SMITH JR., A. Surg. Lieut. (j. g.) U. S. Navy, Alva, Okla., to Miss Louise Evangeline Mack of Charleston, S. C., in June.

SANFORD LAMAR BAILEY, Kosciusko, Miss., to Miss Ruth Elizabeth Williams of Mobile, Ala., in Spartanburg, S. C., June 20.

JOHN GEORGE FEDER, A. Surg. Lieut. (j. g.) U. S. Navy, Pensacola, Fla., to Miss Virginia Heard of Atlanta, Ga., June 25.

JOSIAH CLAYTON CARMICHAEL, Birmingham, Ala., to Miss Ruth Kyle Dale at Nashville, Tenn., June 27.

WALTER DARLINGTON HASTINGS JR. to Miss Frances Goldsmith Black, both of Durham, N. C., in June.

JAMES A. FERGUSON, Grand Rapids, Mich., to Miss Margaret Alice Bevan of Elkhart, Ind., in June.

ERNEST WHITMAL FURGURSON, Plymouth, N. C., to Miss Clara Louise Jones of Red Springs in June.

JAMES T. ROGERS, Fort McPherson, Ga., to Miss Miriam L. McKinney of Greenwood, S. C., in June.

STUART N. MICHAUX, Richmond, Va., to Mrs. Ruth Ann Wolfe Benjamin of New York recently.

HAROLD MILTON SMITH, Savannah, Ga., to Miss Madelyn Elizabeth Meredith of Augusta in June.

HENRY EDWARD PLENGE, Charleston, S. C., to DR. RUTH TALLEY SANDERS of Columbia in June.

DAVID BENJAMIN WILSON, McComb, Miss., to Miss Sara Barry Gillespie at Jackson in June.

JOHN L. CASSIDY, Evansville, Ind., to Miss Mary Ann Hickey of Covington, Ky., May 11.

JOHN BERNARD PLUM, Grand Rapids, Mich., to Miss Suzanne Wells of Nashville, Tenn., in June.

FREDERICK E. KREDEL, Charleston, S. C., to Miss Constance Orme in Nashville, Tenn., June 22.

SCOTT LA RUE TARPLEE, Providence, R. I., to Miss Mimi O'Beirne of Atlanta, Ga., in June.

MYRON A. WALKER, Lafayette, La., to Miss June Grace Blevins of St. Francisville in June.

JOSEPH FREDERICK HASLINGER to Miss Dorothy Jerrine Smith, both of Portland, Ore., May 23.

EUGENE R. BENEDETTO, Alliance, Ohio, to Miss Sylvia Zallanta of Columbus, April 27.

LEONARD MARTIN THOMPSON, Lena, Ill., to Miss Esther M. Grier at Minneapolis, June 20.

VERNON LE ROY BAUER, Andrews, S. C., to Miss Sara Louise Hardy of Hemingway in June.

R. PHILIP RUSK, Cadiz, Ohio, to Miss Marguerite Elizabeth Brodbelt of Columbus, June 8.

WALLIS DICKS CONE, Williston, S. C., to Miss Margaret Dickson of Manning, June 12.

SELWYN H. DRUMMOND, Dayton, Ohio, to Miss Virginia M. Gill of Cincinnati in June.

ROBERT A. EVERHART, Columbus, Ohio, to Miss Gertrude Richardson of Ada, June 14.

THOMAS N. MEADE, Goldendale, Wash., to Miss Roselia C. Turley of Yakima, June 22.

TOBIAS STEIN, Huntington, W. Va., to Miss Martha Landau of Newark, N. J., recently.

EDWARD M. BURNS, Freeport, Ill., to Miss Pauline Elizabeth Hackett of Polo, June 18.

JASPER D. BUSH JR. to Miss Irene Satterfield, both of Birmingham, Ala., June 2.

JOHN PARKS BOOKER to Miss Frances Schumacher, both of Walhalla, S. C., June 17.

LINO J. ARDUINO, Atlanta, Ga., to Miss Elizabeth J. Stemler of Milwaukee, May 22.

MAX R. LONG, Marion, Ind., to Miss Mary McKittrick of Plainville, May 31.

CLAUDE HEARD FORD to Miss Alice Oden, both of Birmingham, Ala., June 1.

JAMES ROWLAND GAY to Miss Lillian Cabell, both of Richmond, Va., July 2.

JOSEPH V. PIRCHIERI to Miss Hortlaine Burns, both of Cleveland, June 8.

H. ROSWELL WAHL, Kansas City, Mo., to Miss Katherine Bell, June 15.

Deaths

Albert Henry Freiberg ✠ Cincinnati, well known as an orthopedic surgeon and as a leader of organized medicine in the state of Ohio, died, July 14, in the Jewish Hospital following an illness of several weeks. He was 71 years old.

Dr. Freiberg was born in Cincinnati Aug. 17, 1868, and received his degree in medicine from the Medical College of Ohio, Cincinnati, later the medical department of the University of Cincinnati, in 1890. Following his graduation he did postgraduate study in Würzburg, Berlin, Strasbourg and Vienna and took up the practice of medicine in Cincinnati in 1893. From 1902 to 1938 he was professor of orthopedic surgery at the University of Cincinnati College of Medicine and since 1902 devoted his time fully to that specialty, serving as consulting orthopedic surgeon to the Cincinnati General and the Children's Hospital and as director of the orthopedic service of the Jewish Hospital. He was elected president of the American Orthopedic Association in 1910 and was chairman of the Section on Orthopedic Surgery of the American Medical Association, 1917-1918. In 1923 he was elected president of the Academy of Medicine of Cincinnati and in 1929 president of the Ohio State Medical Association. His affiliations in scientific organizations included fellowship in the American College of Surgeons and in the American Academy of Orthopedic Surgery as well as in the other organizations which he served as a leader. He gave freely of his time to many civic affairs, holding among other appointments that of member of the Advisory Committee on Crippled Children for the Children's Bureau of the United States Department of Labor. He was a member of the board of trustees of the Cincinnati Institute of Fine Arts and a member of the board of governors of the Hebrew Union College. On Dec. 6, 1939, the president of the University of Cincinnati and the faculty of the College of Medicine sponsored a dinner in honor of Dr. Freiberg.

In 1915 Dr. Freiberg was awarded an honorary LL.D. degree by Cedarville College. He was recognized as a competent amateur botanist and photographer. He played first violin in a string quartet which had met weekly for more than thirty years. He had contributed more recently of his efforts to the work of the Georgia Warm Springs Foundation and of the National Foundation for Infantile Paralysis. His death was recognized by editorial comment in Cincinnati newspapers, which pointed particularly to his sense of social obligation and to his innumerable contributions of service to the poor.

John Gerald FitzGerald, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1903; professor of hygiene and preventive medicine, dean from 1932 to 1936 and lecturer in bacteriology from 1909 to 1911 at his alma mater; director of the School of Hygiene and of Connaught Laboratories, University of Toronto; associate professor of bacteriology at the University of California, Berkeley, from 1911 to 1913; in 1936 was appointed a member of the Permanent Commission on Biological Standardization of the Health Organization of the League of Nations; member of the American Association of Pathologists and Bacteriologists and the Society of American Bacteriologists; fellow of the American College of Physicians; was a scientific director of the International Health Division of the Rockefeller Foundation; in 1937 was a Chadwick lecturer in London; served during the World War; author of "Practice of Preventive Medicine"; aged 57; died, June 20.

Francis Randall Hagner ✠ Washington, D. C.; Columbian University Medical Department, Washington, 1894; professor of genito-urinary surgery from 1905 to 1939, when he became emeritus professor at his alma mater, now known as the George Washington University School of Medicine; past president of the Medical Society of the District of Columbia, the American Association of Genito-Urinary Surgeons and the Clinical Society of Genito-Urinary Surgeons; member of the Southern Surgical Association and the American Urological Association; fellow of the American College of Surgeons; attending genito-urinary surgeon to the George Washington University and Garfield Memorial hospitals; consulting genito-urinary surgeon to the Children's and Gallinger Memorial hospitals; aged 67; died, July 7.

Elsworth Striker Smith ✠ St. Louis; St. Louis Medical College, 1887; an Affiliate Fellow of the American Medical Association; member of the House of Delegates of the American Medical Association in 1920; clinical professor of medicine at his alma mater, now the Washington University School of Medicine, from 1899 to 1923, professor of clinical medicine in 1924 and later professor of clinical medicine emeritus; past president of the St. Louis Medical Society and the St. Louis Society of Internal Medicine; fellow of the American College of Physicians; aged 76; physician to St. Luke's Hospital; consulting physician to St. Louis Maternity Hospital and Barnard Free Skin and Cancer Hospital; associate physician to the Barnes Hospital, where he died, June 6, of carcinoma of the stomach.

William Albert Evans ✠ Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; formerly associate professor of roentgenology at the Detroit College of Medicine and Surgery; fellow of the American College of Physicians; member of the executive council and past president of the American Roentgen Ray Society; member of the Radiological Society of North America, Inc., and the American College of Radiology; for many years president of the city board of health; roentgenologist to the United States Marine Hospital and the Harper Hospital; aged 63; died, June 9, of coronary occlusion.

Rexwald Brown ✠ Santa Barbara, Calif.; Northwestern University Medical School, Chicago, 1903; member of the Western Surgical Association; formerly vice president of the Pacific Coast Surgical Association; fellow of the American College of Surgeons; past president of the Southern California Medical Association and the Santa Barbara County Medical Society; chairman of the city board of health from 1930 to 1934; veteran of the Spanish-American and World wars; for many years director of the surgical division and chairman of the executive committee of the Santa Barbara Cottage Hospital; aged 62; died, June 21, of cerebral hemorrhage and hypertension.

Ben Witt Key ✠ New York; University of Pennsylvania School of Medicine, Philadelphia, 1909; member of the American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society and the Association for Research in Ophthalmology, Inc.; fellow of the American College of Surgeons; formerly instructor of ophthalmology at the University and Bellevue Hospital Medical College; surgeon to the New York Eye and Ear Infirmary; consulting ophthalmologist to the French and Lutheran hospitals; aged 56; died, June 5, in the Presbyterian Hospital.

William Morris Butler, Brooklyn; College of Physicians and Surgeons, medical department of Columbia College, New York, 1873; professor of mental diseases at the New York Homeopathic Medical College and Flower Hospital, New York, from 1904 to 1917; member of the state board of medical examiners from 1892 to 1903; formerly neurologist to the Cumberland Street Hospital and consulting alienist to the Middletown (N. Y.) State Homeopathic Hospital; aged 90; died, June 22, of senility.

Reese Williams Patterson ✠ Knoxville, Tenn.; University of Louisville (Ky.) Medical Department, 1911; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served during the World War; consulting otolaryngologist to St. Mary's Memorial and Fort Sanders hospitals; consulting bronchoscopist to the Knoxville General Hospital; member of the board of directors of the Lincoln Memorial University, Harrogate; aged 57; died, June 24.

Ralph Edwin Stevens ✠ Chattahoochee, Fla.; Jefferson Medical College of Philadelphia, 1915; member of the Southern Psychiatric Association and the American Psychiatric Association; served during the World War; formerly health officer of St. Petersburg; assistant surgeon, Veterans Administration Facility, Bay Pines, from 1932 to 1935; chief physician to the Florida State Hospital; aged 49; died, June 6, in Sanford of acute dilatation of the heart.

Raymond Tillotson Smith, Fort Smith, Ark.; Loyola University School of Medicine, Chicago, 1926; fellow of the American College of Surgeons; secretary-treasurer and past president of the Arkansas Hospital Association; attending ophthalmologist and otorhinolaryngologist to Sparks Memorial Hospital; on the staff of St. Edward's Mercy Hospital; aged 46; died, June 2, of injuries received in an automobile accident.

Ferdinand Gisler Angeny, Avon by the Sea, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1892; served during the World War; formerly bank president; for many years a member of the surgical staff and formerly member of the board of governors of the Royal Pine Hospital, Pinewald, and the Dr. E. C. Hazard Hospital, Long Branch; aged 70; died, June 21, of heart disease.

Samuel James Waterworth ✠ Clearfield, Pa.; College of Physicians and Surgeons, Baltimore, 1893; member of the House of Delegates of the American Medical Association 1917, 1926, 1928; fellow of the American College of Surgeons; past president of the Clearfield County Medical Society; for many years on the staff of the Clearfield Hospital; aged 66; died, June 6, of myocarditis.

Walter Frederick Martin ⊕ Battle Creek, Mich.; American Medical Missionary College, 1903; member of the American Urological Association; fellow of the American College of Surgeons; past president of the Calhoun County Medical Society; urological surgeon to the Battle Creek Sanitarium; aged 65; died, June 11, of lymphosarcoma of the heart.

Harry Addison March, Canton, Ohio; Columbian University Medical Department, Washington, D. C., 1901; served during the World War; formerly county coroner; was known as the "father of professional football," having organized the New York Giants and the Canton Bulldogs; aged 61; died, June 10, of uremia and chronic nephritis.

Harry Hymen Tanzer ⊕ East St. Louis, Ill.; St. Louis University School of Medicine, 1926; assistant in gynecology and obstetrics at his alma mater; on the staffs of Christian Welfare Hospital and St. Mary's Hospital; aged 40; died, June 10, in St. Mary's Hospital, St. Louis, of carcinoma of the intestine.

William Napier Macartney ⊕ Fort Covington, N. Y.; University of the City of New York Medical Department, 1888; past president of the Franklin County Medical Society; for many years county coroner; author of "Fifty Years a Country Doctor"; aged 78; died, June 15, of cerebral hemorrhage.

Paul F. Vasterling, Los Angeles; St. Louis Medical College, 1883; member of the Missouri State Medical Association; fellow of the American College of Surgeons; formerly chief surgeon at the Missouri Railway Hospital, St. Louis; aged 77; died, May 31, of carcinoma of the stomach.

George Benjamin Brown, Dyersburg, Tenn.; Memphis (Tenn.) Hospital Medical College, 1899; member of the Tennessee State Medical Association; served during the World War; aged 65; died, June 23, in the Methodist Hospital, Memphis, of uremia.

Frederick James Bruce, Brooklyn; Long Island College Hospital, Brooklyn, 1887; formerly a surgeon in the police department; aged 74; for many years on the staff of the Good Samaritan Hospital, where he died, June 10, of cerebral hemorrhage.

James Andrew Long, Frederick, Md.; Maryland Medical College, Baltimore, 1903; member of the Medical and Chirurgical Faculty of Maryland; past president of the Frederick County Medical Society; aged 60; died, June 19, of heart disease.

Cecile Markowitz, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1929; member of the board of the Child Welfare Council of Canada; aged 44; on the staff of the Women's College Hospital, where she died, May 14.

Bert Trippeer ⊕ Dwight, Ill.; University of Louisville (Ky.) Medical Department, 1894; Barnes Medical College, St. Louis, 1895; aged 68; died, June 7, in the Grant Hospital, Chicago, of mesenteric thrombosis.

Frank Dunn Mabry ⊕ Port Arthur, Texas; University of Texas School of Medicine, Galveston, 1911; served during the World War; aged 51; died, June 8, in the Nix Hospital, San Antonio, of cerebral hemorrhage.

Ben Clark Gile, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1897; served during the World War; aged 66; died, May 18, in the Presbyterian Hospital of coronary thrombosis.

Herman Janss, Los Angeles; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1899; aged 64; died, May 11, in St. Vincent's Hospital of cardiac infarction.

Leland Eldorus Phipps ⊕ Youngstown, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1908; served during the World War; aged 55; died, June 2, of coronary occlusion.

Joseph Goodwillie Walker, Wichita, Kan.; University of Nebraska College of Medicine, Omaha, 1903; member of the Kansas Medical Society; aged 64; died, May 5, of coronary occlusion.

William Neumann, New York; Columbia University College of Physicians and Surgeons, New York, 1903; aged 66; died, May 27, in Rye, N. Y., of arteriosclerosis and thrombosis.

William R. Owens ⊕ Glendale, Calif.; Memphis (Tenn.) Hospital Medical College, 1903; aged 63; died, June 7, in the Dickson Memorial Hospital, Paragould, Ark., of heart disease.

Barton Jones Farr, Glen Allan, Miss.; University of Louisville (Ky.) Medical Department, 1898; served during the World War; aged 67; died, May 1, of pulmonary tuberculosis.

Arthur Gilbert Holbrook, Coldwater, Mich.; Jefferson Medical College of Philadelphia, 1899; member of the Michigan State Medical Society; aged 73; died, June 5, of thrombosis.

Samuel Goodman, Boston; University of the City of New York Medical Department, 1889; member of the Massachusetts Medical Society; aged 75; died, May 28, of arteriosclerosis.

James L. Morton, Shelbyville, Tenn.; University of Tennessee Medical Department, Nashville, 1903; county health officer; aged 60; died, May 31, of cerebral hemorrhage.

Robert Carl Van Buren, Carey, Ohio; Eclectic Medical Institute, Cincinnati, 1901; member of the Ohio State Medical Association; aged 63; died, May 31, of heart disease.

Albert L. Corcoran ⊕ Peoria, Ill.; Northwestern University Medical School, Chicago, 1892; aged 70; died, June 3, in the Methodist Hospital of cerebral hemorrhage.

Hannah Yoseph Jacobs, Yonkers, N. Y.; New York Medical College and Hospital for Women, New York, 1894; aged 70; died, May 12, of chronic myocarditis.

Henry Osborn Carrington, Santa Barbara, Calif.; University of the City of New York Medical Department, 1894; aged 82; died, May 28, of coronary occlusion.

Walter John Leo O'Brien ⊕ Boston; Harvard Medical School, Boston, 1898; aged 66; died, May 1, in the Baker Memorial Hospital of intestinal obstruction.

Eugenie Louise Gagnon, Providence, R. I. (licensed in Rhode Island by years of practice); aged 74; died, June 11, of diabetes mellitis and chronic nephritis.

John Hamilton McCoy, Alliance, Neb.; Rush Medical College, Chicago, 1902; aged 63; died, May 17, in St. Joseph's Hospital of cerebral hemorrhage.

Walter Seip Freeman, Philadelphia; Jefferson Medical College of Philadelphia, 1901; formerly a pharmacist; aged 80; died, May 15, of myocarditis.

Walter Howard Fox, Hartford, Mich.; National Medical University, Chicago, 1902; also a dentist; aged 82; died, June 6, of carcinoma of the prostate.

Ralph Pool Grimm ⊕ Farmington, Ill.; St. Louis College of Physicians and Surgeons, 1909; aged 54; was killed, June 23, in an automobile accident.

Robert Acheson Hawthorne, Braddyville, Iowa; Omaha Medical College, 1901; aged 72; died, May 15, in Clarinda of cerebral hemorrhage.

Monroe Thomas Koons, Mulberry, Ind.; Long Island College Hospital, Brooklyn, 1878; aged 91; died, May 14, of chronic myocarditis.

David S. Rowland, Miami, Fla.; Baltimore Medical College, 1893; aged 71; died, May 17, of coronary occlusion and arteriosclerosis.

Nicholas Lawrey, Brooklyn; Maryland Medical College, Baltimore, 1900; aged 69; died, June 7, of chronic myocarditis and arteriosclerosis.

Hiram Clark Moorman, Somerville, Tenn.; Louisville (Ky.) Medical College, 1903; aged 64; died, May 17, of coronary occlusion.

Erich Eisner, New York; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, 1911; aged 52; hanged himself, May 7.

M. Willard Bigelow, Payson, Utah; College of Physicians and Surgeons, Baltimore, 1911; aged 64; died, May 21, of angina pectoris.

Andrew J. Shores, Los Angeles; University of Louisville (Ky.) Medical Department, 1888; aged 75; died, May 24, of heart disease.

Casper Franklin Jones, Baltimore; Baltimore Medical College, 1895; aged 76; died, May 27, of carcinoma of the prostate.

William Wallace Cook, Los Angeles; Rush Medical College, Chicago, 1898; aged 67; died, June 2, in an automobile accident.

Robert A. Ware, Chicago; Meharry Medical College, Nashville, Tenn., 1910; aged 56; died, May 16, of a gunshot wound.

Robert William Butler, Orlando, Fla.; Rush Medical College, Chicago, 1876; aged 85; died, June 3, of arteriosclerosis.

Frank Lansing Birney, Denver; Rush Medical College, Chicago, 1883; aged 80; died, June 11, of cardiac decompensation.

Boise S. Bomar, Atlanta, Ga.; Atlanta School of Medicine, 1908; aged 55; died, June 4, of coronary occlusion.

Correspondence

HAY FEVER IN CHICAGO

To the Editor:—Two articles have recently appeared in The Journal which seem to cast doubt on my ability to diagnose hay fever, without offering an iota of fact for the doubt expressed. In the first article, "Potassium Chloride in Allergic Disorders," by George F. Harsh and Paul B. Donovan (May 11, p. 1859), the expressed doubt of my ability to diagnose hay fever was definitely but not too strongly expressed. I quote: "It should be noted that this work was done in Chicago, and the treatment in all these cases was begun on or after Oct. 21, 1938, so that it is highly improbable that any of these patients were suffering from true pollinosis at the time the study was made." This quotation appearing in a highly regarded scientific journal expresses the improbability of my ability to diagnose hay fever but is not backed by scientific facts. My pride was slightly wounded by this unsubstantiated attack on my diagnostic ability, but world events seemed to outweigh my diagnostic acumen so far that I did not take my pen in hand in my defense.

Much to my surprise, on perusing a more recent copy of The Journal I came on a more severe attack on my ability to diagnose hay fever. Rubin, Aaronson, Kaplan and Feinberg, in an article entitled "Potassium Salts in the Treatment of Pollinosis" (June 15, p. 2359), have the following to say with regard to my diagnostic ability: "Fortunately, the author [Abt] included the dates on which the treatment was begun in the individual patient. It is interesting to note that in the seasonal cases of asthma and hay fever the earliest date on which this medication was administered was October 20. Since it is well known that pollinosis in Chicago terminates before the end of September, it is readily apparent that the conclusions are based on false premises. Had Abt failed to give any dates, which is the case with most authors, this report might have been considered substantial evidence in favor of potassium chloride."

The learned authors who produced this quotation and who state that my conclusions are based on false premises offer no fact or scientific proof that the patients whom I observed were or were not suffering from hay fever. In fact, they have themselves fallen into a grievous error or misconception, for they state that "pollinosis in Chicago terminates before the end of September." Probably many of their patients wish that this statement were a fact. Certainly most of my hay fever patients and my friends and acquaintances and many of my colleagues' patients, friends and acquaintances wish that this statement were a fact.

By definition, hay fever occurs when sufficient pollen causes the symptoms in a sensitive person; this may happen in the middle of August, the middle of September, the middle of October, the middle of November or the middle of any month when pollen and the sensitive individual meet. It would hardly seem necessary to quote authority for this fact.

French K. Hansel (Allergy of the Nose and Paranasal Sinuses, St. Louis, C. V. Mosby Company, 1936, p. 730), in discussing atmospheric studies in the United States and Canada in relation to pollen, under "North Central States" (in which area studies from Chicago are included), notes that "ragweeds are by far the most important sources of pollen in Illinois." He further states: "In Chicago and surrounding cities on the lake the direction of the wind is more important than its velocity." A final quotation from Hansel's book should suffice; strangely enough, Dr. Feinberg is given as one of the authors for the authority of the following quotation—evidently he has forgotten some of his earlier writings. On page 691 he says: "According to Feinberg and Durham, unusual weather conditions may change the relative severity of the hay fever season and transform a plant ordinarily considered as harmless into an important cause of hay fever." Nowhere in this complete review by Hansel on pollinosis in the Chicago area is the statement made that pollinosis terminates before the end of September.

I should like to present some facts which will purport to show that there was pollen in the air in Chicago in October 1938. In a report obtained through the kindness of O. C. Durham on the pollens found in Chicago during October 1938, the ragweed counts given in the table were noted by him for the following dates (it should be noted that these counts were made from plates exposed on the roof of the courthouse in Chicago, which is in the loop district, and that in all probability if counts had been made in outlying areas, which are in closer proximity to weeds and grasses, such counts would have been higher). Again quoting from Hansel (p. 690): "In 1926 Koessler and Durham made complete field and atmospheric studies of the hay fever causing pollens in 171 mile-square blocks in Chicago and vicinity, and it was found that 38 per cent of the total area is allowed to run to weeds and wild grasses (40,000 acres)."

Thus, through the courtesy of O. C. Durham, I have established the fact that there was ragweed pollen in the air in Chicago in October 1938 and, since my patients lived in Chicago and were sensitive to these pollens and had the classic symptoms of hay fever, my diagnosis was correct.

Botanists teach us, even in our elementary courses, that plants may grow and pollinate until frosts lay them low. This statement is a basic fact and needs no proof. Through the courtesy of C. A. Donnel of the United States Department of Agriculture, Weather Bureau, I have obtained the monthly meteorologic summary for Chicago for October and November 1938; the authors of the two articles, to whom I am addressing this communication, may obtain similar copies of this meteorologic summary. In the report from the weather bureau for October 1938 no heavy or killing frosts were reported for October 1938. The lowest minimum temperature for the month was 35 F., on October 23 and 24; there was a light frost on October 25 and no heavy or killing frosts reported for October 1938. The average date for the first killing frost of the autumn in Chicago is given as October 19. The report for November 1938 states that the first killing frost occurred November 8.

Report of Pollens Found on Atmospheric Slides, Chicago, October 1938

	Ragweed
October 3	2
4	10
5	5
7	2
10	5
11	2
12	3
14	4
16	1
17	1

My thirteen hay fever patients, with one exception, were all seen before the evening of November 8, and the one exception was seen on November 9. The prevailing wind was from the south and southwest for the first half of November, and the wind from this direction sweeps over the prairies and brings the pollen directly into Chicago. These are the facts.

It is interesting to note that Feinberg and his associates report that they made daily pollen counts, and they state in their conclusion: "Reports of therapeutic results in hay fever should be received with skepticism unless they bear the earmarks of evaluation by methods based on relationship of the symptoms to daily, seasonal and geographic fluctuation of the pollen counts." Fortunately in Chicago, through the courtesy of the Abbott Laboratories, daily pollen counts are made by O. C. Durham and are published in the daily newspapers. These accounts are also kept on file, and it would have been quite as

easy for the authors of these two papers to obtain them as it was for me, even after a lapse of eighteen months.

In my article "Note on Oral Administration of Potassium Chloride in the Treatment of Hay Fever, Nasal Allergy, Asthma and Sinusitis" (*Am. J. M. Sc.* **198**:229 [Aug.] 1939) I state: "Potassium chloride should not be given in capsules, tablets or powder, in undiluted form. Sodium chloride intake should be limited during the period of treatment." Harsh and Donovan state: "A 5 grain capsule of potassium chloride was given with each meal and sodium chloride was not restricted. Those who experienced gastrointestinal irritation were asked to sprinkle the powder on their food or dissolve it in a glass of water." They state that, although they did not see the logic in following my method of therapy, they adopted it. I would be so bold as to state, and the reader may judge for himself, that the authors did not restrict sodium chloride as advised by me and used on my patients and they did use potassium chloride as a powder in undiluted form and not as I used the potassium chloride in dilution, and therefore I would conclude that they did not adopt my method of therapy.

Recent reports (Rusk, H. A.; Dean, L. W., Jr., and Rindskopf, Wallace: Results of Potassium Therapy in Nasal Allergy, *Ann. Otol., Rhin. & Laryng.* **49**:76 [March] 1940; Kern, R. A.: The Role of Water Balance in the Clinical Manifestations of Allergy, *Am. J. M. Sc.* **199**:778 [June] 1940) indicate some degree of success in the treatment of pollinosis with potassium chloride. Rusk obtained 33 per cent relief of some degree in thirty patients suffering with ragweed pollinosis. He further says "These patients were all advised to reduce materially the amount of sodium in their diet." Kern states that "By no means all patients, not even a sizeable minority, were helped by potassium chloride alone. The addition of potassium chloride to other types of therapy distinctly improved results in some cases." He further states that "Increased intake of potassium, or decreased intake of sodium, by tending to increase intracellular fluid and to decrease interstitial fluid and edema, will antagonize allergic reactions."

The only object I had in publishing my note on potassium chloride in the treatment of these conditions was to call attention to its availability and to hope that future reports would prove or disprove its merits. I believe that I have accomplished my purpose, as nearly every recent issue of all the first class medical journals in this country seem to have an article on the use of potassium chloride in pollinosis, either for or against. Most of the articles are fair; the two which I have here taken exception to, in that they challenged my ability to diagnose hay fever, seem to me to have been conceived by their authors on the "improbability" and "false premise" that potassium chloride ought not to give results of a positive therapeutic nature; that they did not wish their patients to benefit by this therapy, and they seem to have tried to prove that they did not.

ARTHUR F. ABT, M.D., Chicago.

DEATHS FOLLOWING MAPHARSEN THERAPY

To the Editor:—In their article "Mapharsen in Treatment of Syphilis in Office Practice" in THE JOURNAL, Nov. 25, 1939, Rein and Wise mention that "there is not a single recorded instance of aplastic anemia or death which could be attributed to mapharsen." May I kindly call your attention to the article in the *Indian Medical Gazette* (January 1939, p. 24) by Drs. Rajam and Rao of the Venereal Department, General Hospital, Madras, in which they have recorded two deaths, one due to granulocytopenia and the other due to encephalitis following mapharsen therapy.

P. N. RANGIAH, M.B., B.S., Madras, India.
Honorary Assistant Medical Officer, Venereal Department, Government General Hospital.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

LUBRICATING OILS AND PULMONARY DISEASE

***To the Editor:*—What deleterious results may ensue in the lungs or tracheobronchial tree from inhalation of a fine mist of oil droplets thrown off from grinding machines in the process of centerless grinding? The cutting oil used is a sulfurized mineral oil containing no halogens. Can changes similar to those of the lipid pneumonias occur from repeated exposures in an eight hour working shift? Over a period of many years no harmful results are known among a large group of employees. However, the question has arisen owing to the recent complaint of an employee of cough and shortness of breath after an exposure to such an atmosphere in the grinding room.**

M.D., Ohio.

ANSWER.—Sulfurized mineral oil in distinction to sulfonated mineral oil is an oil containing uncombined sulfur, usually only to the extent of 2.5 per cent but under special conditions up to 5 per cent. Owing to the heat of friction, traces at least of sulfur dioxide may be formed in some industrial operations. Although slight irritation has been noticed, severe injury has not been recorded. In the case of vegetable oils the content of added sulfur may be as high as 10 per cent, thus paving the way for greater amounts of sulfur dioxide. Low concentrations such as 10 or 20 parts per million of air may provoke coughing. Prolonged exposures to sulfur dioxide have been associated with the production of bronchiectasis. Many thousands of workers daily are exposed to lubricating and cutting oil mists without the development of such pathologic states as to attract attention, with the exception of cutaneous lesions. Oil nuclei reaching the terminal air sacs may interfere with gaseous exchange and thus lead to anoxia. However, the quantity of oil in the particle size that will float in the air is so little that the total entering the lung is trivial. Irritation of the respiratory tract from oil mists may arise if the oil contains impurities or if under the action of such agencies as heat has broken down with formation of decomposition aldehydes or the like. Pulmonary cancer has been attributed to lubricating oils but the evidence is doubtful (Touraine, A., and Bour, H.: *Rev. méd. franç.* **20**:285 [April] 1939). Unfortunately, pathologists have not directed enough attention to the problem of oil aspiration in industry, and clinicians have made little study of the problem. Much attention has been paid to dusts, but not so much to oil inhalations. Nevertheless, mineral oil is an irritant in the lungs and certainly does no good, even though the harm usually is not great.

MASSIVE DOSE OF VITAMIN D FOR RICKETS

***To the Editor:*—Has the massive dose of vitamin D (600,000 international units), given subcutaneously or orally, been proved to prevent or cure rickets? Would you advise preventive treatment of rickets by a single injection of this dose given in the fall months? Is it possible that toxic reactions will develop following the single massive dose of the vitamin D? Are commercial preparations available that will permit such large doses?**

M.D., New York.

ANSWER.—Rickets can be cured by giving a single dose of 600,000 international units of vitamin D, administered orally in milk. The administration of the vitamin subcutaneously or intraperitoneally has been performed in rachitic rats and on one or two occasions experimentally in the human infant. Altogether there are recorded in the literature approximately 150 children to whom such massive doses of vitamin D have been administered orally.

Recent reports have shown that moderate and severe rickets have been cured by administering 800 units of vitamin D daily, with signs of healing at the end of the first week of therapy and with complete cure at the end of six weeks; a total dosage of one twentieth the amount of the single massive dose accomplishes the same result a little more slowly.

Toxic symptoms have been reported in adults suffering from arthritis with massive doses of vitamin D. It is claimed that the toxicity is due to by-products rather than to the pure vitamin itself.

The use of these massive doses is still in the early experimental stage. The general adoption of this method should certainly await more carefully controlled and more extensive clinical experience. Certain commercial laboratories have preparations with high vitamin D potency.

The availability of the concentrated preparations of vitamin D may tempt the investigator to use massive doses. It should not be forgotten that in using large doses one may, besides the ordinary vitamin effect, be eliciting a drug effect. For the present, at least until the pharmacology of massive doses is more clearly understood, their use should be limited to carefully conducted, well chosen clinical trial.

STERILITY

To the Editor:—**A woman aged 28, married three years, has been unable to conceive. The spermatozoa of the husband are numerous, freely motile and of normal size and shape. No contraceptive practices have been used. The woman is healthy and has always been in excellent physical and mental health with the exception of a vague, mild abdominal complaint diagnosed by the doctor as "a sensitive appendix," which she had about six years ago and which did not bother her except to cause a bit of pain for a couple of days. There is no history or evidence of venereal disease in either partner. Insufflation of air into the uterus a month ago caused considerable pain in both shoulders about twenty minutes after the manipulation, lasting about an hour. I take it that this pain in the shoulders was due to irritation of the peritoneum by the air that had gradually risen to the upper part of the abdominal cavity when the patient assumed the upright position. The pain affected the shoulders at about the same time but there was a distinct short interval between the onset in each shoulder, pain in the one shoulder coming on about five minutes after it had come on in the other. Inspection of the cervix shows no abnormality. The menstrual history is that for a day or two just before the menses she has some mild cramplike pains, which subside after a few minutes and recur at intervals of a few hours. Thus after a day or two of freedom, the menses begin. Pain is sometimes severe and yet at other times is lacking altogether. Usually the clots are large. Considerable medication has to be administered to obtain relief from the cramps when the period happens to be a painful one. The flow lasts from three to four days. The menses have always been regular since their inception, except rarely, when they begin a day or two before the expected date. There does not appear to be any endocrine dysfunction that can be detected by simple clinical procedures, but the gynecologist who did the air insufflation suggested that perhaps a reading of the basal metabolic rate might show up some vague thyroid insufficiency, although he was only lukewarm in recommending the procedure. 1. Can one assume that the oviducts are patent? Is the assumption of air irritating the peritoneum correct for explaining the pain in the shoulders? 2. Would a basal metabolic test be of any use in such a case? Would some small doses of thyroid be of any use, hoping to favor alteration of her endocrine system, in attempts to get her to conceive? Is such careful medication wise if the basal metabolic rate is not determined? 3. What is the status of such preparations as gonadogen (Upjohn) in cases of this kind? Might there be any adverse effects from such medication without any blood studies being made before medication? What common untoward results may accrue from this type of medication? 4. What other common factors may be responsible for such sterility? 5. To what extent, if any, does vaginal acidity play a part in such cases? Would douching be of any use? If so, with what?**

M.D., Indiana.

ANSWER.—1. One can safely assume that in this case the oviducts are patent or at least that one of them is open. The pain in the shoulders following the Rubin test is due to irritation of the abdominal surface of the diaphragm by the gas or air which escapes from the oviducts and forms a subphrenic pneumoperitoneum. Pain in the shoulder also occurs when blood from a ruptured ectopic pregnancy accumulates under the diaphragm producing a subphrenic hemoperitoneum. Likewise in cases of purulent peritonitis following rupture of the appendix, shoulder pain may occur.

2. One or more basal metabolism tests should be made in this case because such tests should be performed as a routine in all cases of unexplained sterility. If the basal rate is low, thyroid medication is indicated. Some sterile women have a low basal metabolic rate and a large proportion of them become pregnant after thyroid administration. Even in the presence of a normal basal rate, small doses of thyroid (from one-half to 1 grain [0.03 to 0.06 Gm.] daily) may be helpful; but all women who are receiving thyroid therapy should have repeated basal metabolism studies made, preferably once a month. It is hazardous to continue thyroid medication for a long time without checking the basal rate from time to time.

It is generally assumed that women who menstruate with the usual degree of regularity and in whom one or more biopsies reveal secretory endometrium ovulate every month. Such women do not require gonadotropic therapy. In fact, the gonadotropin may do more harm by producing excessive follicle stimulation, but this is temporary. If, on the other hand, endometrial biopsy performed just before or on the first day of the menses shows a proliferative type of endometrium, this is evidence that ovulation failed to take place. In such an event more gonadotropin may be administered in the hope that it will stimulate ovulation. It must be remembered that this form of therapy is still highly experimental for human beings and there is no satisfactory evidence that ovulation can be induced in an abnormal ovary. Furthermore, gonadotropin is an equine serum and precautions must be taken by cutaneous testing to avoid a serious reaction. It must also be borne in mind that some women who do not ovulate at certain times do have ovulation at other times and hence there may be a spontaneous cure of absence of ovulation.

4. It is difficult to explain some cases of sterility when both husband and wife are apparently normal in every way. Occasionally a simple occurrence such as a temporary change of climate by taking a trip results in a pregnancy. In other instances, after many years of marriage with apparently no change in health, routine of living or other conditions, conception occurs for no explainable reason.

5. Vaginal acidity has practically nothing to do with sterility. Hence douches are of questionable value in spite of the conceptions which occasionally are attributed to various douches.

ARTHRITIS AND ESTROGENS

To the Editor:—**Information is requested as to whether or not cases of arthritis (rheumatoid) have been caused or have occurred coincidentally with the use of estrogenic substances. If such have occurred, references to the literature would be appreciated.**

W. S. Douglas, M.D., Lewiston, Idaho.

ANSWER.—A survey of the literature on arthritis reveals no evidence to indicate that rheumatoid or any other form of arthritis of man is due to the estrogenic hormone. Indeed, the idea is held by some that certain forms of arthritis, for example menopausal or villous arthritis and perhaps also hypertrophic (osteo-) arthritis, are related to a deficiency, not an oversufficiency, of the estrogenic hormone. Hall, Radnor and others have treated these with estrogenic substance and have reported some amelioration of articular symptoms in cases of "menopause arthralgia" and "typical polyarthritis." However, the Silberbergs recently reported that estrogen, administered to immature guinea-pigs over periods of from three to sixty days, caused retrogressive changes, increased hyalinization and ossification of the intercartilaginous ground substance in the epiphysial disks, ribs and vertebrae. The cartilage cells respond with temporary cessation of growth and differentiation, followed by degenerative changes and subsequent proliferation and hypertrophy. At present it is not certain that these effects are specific to certain hormones.

References:

1. Hall, F. C.: Menopause Arthralgia: A Study of Seventy-One Women at Artificial Menopause, *New England J. Med.* **219:** 1015 (Dec. 29) 1938.
2. Radnor, Ivor: Polyarticular Arthritis Treated with Estrogenic Hormone, *Brit. M. J.* **1:** 505 (March 11) 1939.
3. Silberberg, Martin, and Silberberg, Ruth: Action of Estrogen on Skeletal Tissues of Immature Guinea Pigs, *Arch. Path.* **28:** 340 (Sept.) 1939.

SPONTANEOUS INTERNAL BILIARY FISTULAS

To the Editor:—**I recently had a patient with a sinus between the duodenum and the cystic duct permitting the barium going by mouth to enter the biliary tree. I have not been able to locate anything of the sort in the literature here. Will you please let me know where I can find something on kindred conditions?**

Hudson Talbott, M.D., St. Louis.

ANSWER.—Spontaneous internal biliary fistulas are infrequent but not rare. Roth, Schroeder and Schloth (cited by Borman et al. 1937) observed this condition in forty-three cases among 10,866 necropsies. Judd and Burden (*Ann. Surg.* **81:**305 [Jan.] 1925) have reported 153 cases of this disorder found at the time of operation. About two thirds of the patients in whom this condition has been observed were women. The fistulous communication in the majority of the cases is between the gallbladder or cystic duct and the duodenum or colon. A few cases have been reported in which the fistula existed between the common duct and the duodenum or colon.

The symptoms associated with internal biliary fistula are varied and usually chronic, frequently including epigastric pain accompanied with or without jaundice and occasionally with chills and fever. The sudden and unusual relief from long standing intermittent gallbladder pain associated with remission of jaundice is highly suggestive of the establishment of internal fistula according to Borman and Rigler (*Surgery* **1:**349 [March] 1937). However, the preoperative diagnosis of this condition depends on the roentgenologic demonstration of either barium or air in the extrahepatic biliary tree and a fistulous communication. Approximately sixty-five such cases have been reported as diagnosed by this means.

The most common cause of these fistulas is a combination of stones associated with chronic infection of the gallbladder. Local ulceration and necrosis usually lead to the formation of the fistula, although erosion of a duodenal ulcer or of a gastric or biliary carcinoma have been known to produce fistulas. Many of these communications will no doubt close spontaneously if no obstruction of the common duct exists distal to the fistula.

It is well recognized that surgical cholecystostomies and cholecystenterostomies nearly always close if the common duct remains patent.

Surgical intervention is indicated in cases of persistent internal biliary fistula, since several serious complications may arise from the continuous regurgitation of intestinal contents into the extrahepatic biliary tree. Operative procedures are designed to relieve the common duct obstruction if possible and then to close the fistulous tract at its intestinal entrance. Judd and Burden recommend cholecystectomy in all feasible cases, since the gallbladder is nearly always severely diseased. However, in cases in which the common duct obstruction cannot be relieved it may be necessary to utilize the gallbladder in establishing a more desirable fistula than the one already present.

EXTENSION DEFORMITY OF LEG IN INFANT

To the Editor:—**Recently I attended a young primipara who was delivered of a set of twins. Both were of the female sex, the first weighing 5 pounds (2,268 Gm.) and the second 5 pounds 13 ounces (2,637 Gm.). Her pregnancy was normal and her labor not significantly unusual, lasting five hours in all, the only variation being that I found it necessary to apply low forceps for extraction of the first fetus after the head was on the perineum for two hours. The indication for forceps was secondary inertia, possibly resulting from the obstetric analgesia (scopolamine and pentobarbital sodium were employed). The first of the twins was found to have an abnormality of the right lower extremity but was otherwise normal. This anomaly seemed to be in the knee joint, the leg lying hyperextended on the thigh so that the anterior surface of the leg would lie against the anterior surface of the thigh. There was also some angulation tending to displace the leg medially so that the toes would point toward and approximate the opposite groin. As far as I can tell there is no bony anomaly and no dislocation of the joint—that is, there is no anatomic variation from the normal when the affected extremity is lined up and compared with the opposite one. Fluoroscopy shows no abnormalities in the bony anatomy and the two extremities appear essentially alike. The leg can be straightened out and flexed, although passive flexion is somewhat restricted as compared to the other side. It is my impression that this congenital defect is the result of malposition in utero, probably the result of pressure from the other fetus, and that the deformity now seen is due to stretching of the posterior capsule and ligaments of the knee joint with some adaptative shortening of the soft structures anteriorly. Incidentally, these are not identical twins, for separate sacs and placentas were present. Two days ago I applied a cast correcting the deformity to that of the normal position, permitting slight flexion (about 15 degrees at the knee joint); also the foot was put up in slight calcaneovalgus position to overcorrect for a slight equinovarus tendency. By this I hope to prevent persistence and exaggeration of the present deformity and possibly to obtain shortening of the posterior capsule and ligaments with resultant restriction of the abnormal mobility. I should greatly appreciate any further suggestions as to treatment, particularly as to whether or not the child should be referred to a specialist without further delay.**

J. M. Spatz, M.D., Glasgow, Mont.

ANSWER.—The clinical description of this case has been excellently given. The theory that deformities noted at birth may be the result of malposition in utero has largely been abandoned in the light of more recent and more complete knowledge of embryology. Although the average fetus changes its position often and moves both arms and legs frequently during the later weeks of pregnancy, the complication of the twin may have resulted in the malposition referred to. Against this hypothesis, however, is the fact that the leg could be readily brought down into anatomic position. Had the leg been hyperextended against the thigh for any length of time, it would be reasonable to expect that the anterior soft tissue structures, including the quadriceps muscle and tendons, would have become shortened.

In all probability the leg was injured at the time of delivery. Hyperextension of the leg at the knee during the progress of the labor or at delivery itself may well have dislocated the distal femoral epiphysis, making it readily possible to place the anterior surface of the lower leg in contact with the anterior surface of the thigh. In a small newborn infant, such an injury at the epiphysis may show poorly or not at all in the roentgenogram. Whether or not this deformity had persisted for some time prior to termination of the pregnancy could be best determined by knowing just how difficult it was to straighten the leg to a normal position and subsequently to flex it.

The treatment which has been used is quite correct. The cast may be bivalved after three weeks and gentle massage, passive and active motion in flexion begun while still protecting the leg against complete extension or hyperextension.

Roentgenograms should be made at monthy intervals until the child is at least 6 months of age in order to watch for the development of the centers of ossification in the epiphyses and to determine any evidence of periosteal new bone formation, which would probably appear after two or three weeks, if the deformity was on a traumatic basis.

If a specialist is available it would be advisable to obtain an opinion. It is doubtful, however, if any fault could be found with the manner in which the infant has been cared for.

LIGATION OF FEMORAL VEIN

To the Editor:—**What will be the immediate and remote effects of tying off the femoral vein accidentally or purposely to prevent bleeding from a tear at the junction of the femoral and long saphenous veins, during a ligation of the long saphenous vein?**

M.D., Massachusetts.

ANSWER.—Ligation of the femoral vein proximal to the saphenofemoral junction unquestionably causes temporary edema and cyanosis. The effects of such sudden venous occlusion can be overcome to a great extent by an immediate block of the lumbar sympathetic chain with procaine hydrochloride; this is because a reflex vasoconstriction accompanying the venous obstruction has much to do with production of cyanosis and edema. The extent of the residual edema will depend on the extent of the ascending and descending venous thrombosis which may follow the tying of the femoral vein. This vein has been repeatedly tied below the profunda because of multiple embolizations; reports are also available of the tying of the vena cava which is compatible with well functioning extremities as long as it occurs distal to the renal vein. A collateral venous network is apt to develop in the gluteal, pudendal and suprapubic regions and obviously should not be obliterated.

For all these reasons a lateral suture of the vein should be attempted if feasible and if suitable suture material is on hand.

SKIN FUNGI AND HYDROGEN ION CONCENTRATION

To the Editor:—**Would you kindly give me some references concerning the *p*H of the skin in fungous infection?**

M.D., New Jersey.

ANSWER.—The following references concern themselves with fungi and hydrogen ion concentration:

Peck, S. M., and Rosenfeld, Herbert: Effects of Hydrogen Ion Concentration, Fatty Acids and Vitamin C on Growth of Fungi *J. Invest. Dermat.* **1**: 237 (Aug.) 1938.

Kadisch, E.: Ueber die Bedeutung der Nährbodenalkalität in der Mykologie, *Dermat. Ztschr.* **55**: 384 (April) 1929.

Huszek, H.: Ueber den Einfluss des "Wassers" der Zusatzsubstanzen und des *p*H Auf die Entwicklung der Pilzkulturen, *Zentralbl. f. Bakt.* (pt. 1) **136**: 120 (Feb. 13) 1936.

Vamos, L.: Pilze und Wasserstoffionenkonzentration, *Dermat. Ztschr.* **63**: 345 (April) 1932.

Talice, R. V.: Le facteur *p*H en mycologie, *Ann. de parasitol.* **8**: 182 (March 1) 1930.

Cerutti, Pietro: Concentrazione idrogenionica e sviluppo degli ifomiceti patogeni, *Pathologica* **25**: 32 (Jan. 15) 1933.

von Mallinckrodt-Haupt, A. S.: Der Wert der *p*H-Messung bei Pilzkulturen, *Zentralbl. f. Bakt.* (pt. 1) **125**: 368 (Aug. 27) 1932.

ALLERGIC HYPOSENSITIZATION

To the Editor:—**What percentage of patients allergic to various proteins are benefited by specific desensitization treatment? As a rule how long does a course of desensitization treatment (protein antigens) give relief in those who are completely relieved?**

D. R. Martin, M.D., Newton, Ill.

ANSWER.—A full treatise on the subject of allergy would be required to answer this question completely. No attempt at hyposensitization should be made if the allergenic substance is avoidable. This is both better and more practical than attempts at hyposensitization. If symptoms are due to substances which cannot be removed from the patient's environment, as pollens, molds and house dust, injection therapy is indicated. The number of injections required for each of these is too variable for practical advice to be given. A few coseasonal injections may be enough in some cases. In other cases from twenty to forty injections may be required to establish a preseasonal dose adequate for relief. The rule is established by the patient and not by the condition. As to the proportion of this group that may be helped, published statistics vary from 70 to 90 per cent of treated patients. It is difficult to establish permanent immunity to any allergic condition. Years of treatment are usually required for the small percentage who are permanently relieved.

The other environmental substances, such as feathers, horse dander, wool and cottonseed, are usually avoidable so that with proper cooperation on the part of the patient treatment by injection is seldom necessary. Hyposensitization is not as satisfactory as with pollens and molds. There are patients who, because of occupational requirements or because of a complicated environment, require injections of such substances as horse dander, cottonseed (dangerous) or feathers, in addition to their complete removal, at least from the bedroom. Such treatment requires extensive experience on the part of the physician. In its absence, the patient is usually better off without treatment.

The injection of food allergens is mentioned only to be condemned. This procedure is seldom necessary, usually ineffective and always dangerous.

PARADOXICAL BREATHING AND RIB RETRACTION IN INFANT

To the Editor:—A child aged 14 months has breathing which has been peculiar since the child was 2 or 3 weeks old. There was some pus in the urine for a while, which cleared up. There has been somewhat of a problem with feeding, which is apparently being satisfactorily adjusted and the child has for some time shown a slow but progressive gain in weight. The child's nervous system appears normal. Breath sounds seem clear on both sides. The heart seems normal. The child has lately developed paradoxical breathing of the anterior inferior half of the chest wall, embodying the lower two thirds of the body of the sternum, xiphoid process and the anterior ends of the lower ribs, drawing in markedly with each inspiration. A diagnosis of fibrosis of the right lung following the use of mild protein silver drops in the nose has been given in this case. I am more inclined to the opinion that there is a congenital disturbance here. I should like to know what possible differential diagnoses should be considered, particularly in relation to this unusual movement of the chest wall.

Philip T. Holland, M.D., Bloomington, Ind.

ANSWER.—The patient presents a picture suggesting an obstruction to the free entrance of air into the lungs with each inspiration. In infants and young children the chondral portion of the ribs is proportionately larger and softer than in older children and adults. Consequently when any narrowing of the airway occurs and the normal negative pressure which is produced by depression of the diaphragm and expansion of the thorax is not being equalized by the ingress of inspired air, a partial vacuum results with the occurrence of certain phenomena in the thorax. The extent of these so-called retractive phenomena depend on the age of the individual and the elasticity of the tissues of the chest and the type of respiration which is normal for that age. The infant's respiration is chiefly abdominal. Abdominal respiration occurs almost exclusively in young infants and gradually changes to the thoracic-abdominal type toward the end of the second year. This change occurs a little earlier in boys. The reason the disturbance in this case apparently has become more marked is that the child has become older and the upper part of the thorax is beginning to expand with inspiration, thereby increasing the negative intrapulmonic pressure with each inspiration.

In view of the mechanics of the respiratory movements, the description presented indicates the presence of some hindrance to inspiration which has apparently been present since birth. Some congenital anomaly of the larynx or trachea such as stenosis of either larynx or trachea, laryngeal webs, relaxation of the aryepiglottic folds or relaxation of the epiglottis. Other conditions which may produce such a sequence of events include mediastinal tumors of a congenital type, such as dermoid cysts or teratoma. In addition, thymus enlargement with tracheal compression should be ruled out. Certainly an x-ray examination of the chest in both the anteroposterior and lateral planes would be of some value in this case and a direct laryngoscopy or bronchoscopy might contribute some pertinent data.

REACTIONS TO SACRAL ANESTHESIA AND PERNICIOUS ANEMIA

To the Editor:—Would you please give me some information on the after-effects of sacral anesthesia performed in the case in question for a rectal operation. The patient developed thereafter slight symptoms indicating involvement of the posterior and lateral columns of the cord with some difficulty in walking and numbness of the lower extremities. The only positive neurologic observations were moderate muscle tenderness in both calves, slight unsteadiness in gait, tenderness on thumping over the sacral spine, absent Achilles jerks, positive Babinski sign on the right and an equivocal Babinski sign on the left. The spinal fluid was under pressure of 150 mm. of water. There was no manometric block. The fluid was clear and colorless and it contained 5 lymphocytes per cubic millimeter. The Pandy and Nonne Apelt reactions were negative; the cerebrospinal Kahn reaction was negative. The colloidal gold curve was 0011000000. The mastic solution curve was flat. There were a trace of globulin and 25 mg. of total protein per hundred cubic centimeters of spinal fluid. No free hydrochloric acid has been found in the stomach after one hour gastric analysis, as a result of which the diagnosis of pernicious anemia has been made. Complete examination has revealed nothing else of importance. Are reactions to sacral anesthesia such as this common?

M.D., Michigan.

ANSWER.—From the experimental and clinical points of view it has been repeatedly demonstrated that spinal anesthesia may be followed by neurologic disorders. These include mild meningeal reactions (leptomeningitis), spinal root lesions (caudal neuritis), more severe meningeal involvement with adhesions to the cord, and occasionally degenerative lesions of the spinal cord. Any one using spinal anesthesia should always be prepared for some complications or sequels. Whenever any substance (liquid, solid or air) is injected into the spinal subarachnoid space a definite meningeal reaction results. The degree and extent of that reaction depend on the strength and quantity of the injected material. These reactions are common but fortunately clear up in the majority of cases. From the objective evidence submitted in this case one can certainly think of a subacute combined degeneration of the spinal cord due to pernicious anemia and not to the sacral anesthetic, especially if the blood picture is characteristic. The patient should be kept at absolute rest and should receive large doses of liver extract parenterally as well as nicotinic acid.

BRITTLE FINGER NAILS

To the Editor:—A woman of 53 for the past several years has had trouble with her finger nails in that they crack longitudinally and tend to break off before they have grown out beyond the quick. Otherwise the patient appears in good health. Could you give me some lead as to etiology and therapy?

M.D., Massachusetts.

ANSWER.—Brittleness of the nails (onychorrhexis) is a malformation of the nail plate and may occur as a sequel of disturbed function of the matrix due to such causes as (1) primary disturbances of nutrition and defective innervation of the matrix, as in cases of paralysis; (2) secondary interference with the function of the matrix from trauma and malformations of the lateral furrow or inflammations of the underlying connective tissue, such as periosteum or bone. The nails may break from slight causes, thus maintaining a partial denudation or continuous irritability of the nail bed. In order to treat the faulty nail formation, an endeavor should be made to remove causes falling in groups 1 and 2, if discoverable, together with use of vitamins A and D and the ingestion of considerable milk to supply calcium. It is well to protect the nail locally by an appropriate pressure bandage made of adhesive tape or wax.

RECURRENT THROMBOSIS AND EMBOLISM

To the Editor:—A woman has been suffering from small painful multiple emboli for the past two years, which have been more frequent recently. Eleven years ago she had thrombophlebitis in both legs following childbirth. For the past nine years she has had large ulcers on the medial surface of both ankles with no evidence of varicosities. During the past six months these have completely healed by the compression type of treatment. I would appreciate any information as to further treatment and prognosis.

M.D., Ohio.

ANSWER.—It is assumed that the correspondent indicates that his patient has had recurrent episodes of pulmonary embolism resulting from venous thrombosis. Because this is an unusual condition, the correctness of the diagnosis should be carefully checked. It is common belief by those who are interested particularly in diseases of the veins that phlebitis is almost never a chronic disease but rather that acute episodes of phlebitis recur. If the case under consideration may be considered an example of recurrent phlebitis with pulmonary embolism, treatment should be directed toward the prevention of recurrence of the phlebitis and venous thrombosis. Unfortunately there is no uniformly successful plan of treatment. However, it is advisable to eradicate foci of infection, to use a vaccine made from organisms cultured from one of the foci, and to have the patient cease smoking if she smokes at the present time. Naturally it is advisable to examine the blood carefully for evidence of dyscrasias which predispose to venous thrombosis.

LOCAL APPLICATION OF SULFANILAMIDE

To the Editor:—I am interested in receiving information on the use of a hot sulfanilamide solution in the treatment of abscess formation.

Frederick L. Scheyer, M.D., Puyallup, Wash.

ANSWER.—F. R. Adams reported at the Greater Philadelphia Dental Meeting, Feb. 1, 1940, good results obtained by the direct injection of a hot sulfanilamide solution into abscesses. There is, however, information available which shows that the local application of crystalline sulfanilamide to infected wounds and open abscesses is a rational therapeutic procedure. Good results have been obtained by the repeated local application of sulfanilamide powder without concurrent oral administration of the drug in infected wounds, superficial ulcers and draining abscesses and sinuses.

HAIR AND PERSPIRATION IN CHINESE

To the Editor:—John Gunther's "Inside Asia," 1939 edition, states on page 285, "Chinese do not perspire; they have no ear wax and very little bodily hair." I have indeed a great deal of respect for Mr. Gunther but believe the Chinese must perspire if not perceptibly.

R. A. Whitney, M.D., White River Junction, Vt.

ANSWER.—It is not known on what authority Mr. Gunther made his statement, but testimony of educated Chinese residing in this country, as well as observation, fails to confirm his statement as to perspiring. It is true that the Chinese have little body hair as a rule and that ear wax seems to be less abundant, but they are present.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, July 20, page 240.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, Sept. 11-13, to be given in medical centers having five or more candidates desiring to take the examination. Part III, Baltimore and New York during October and Boston during November. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various centers, Feb. 20. Final date for filing application is December 21. *Oral.* Cleveland, preceding A. M. A. convention. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written.* Various centers, Oct. 28. Applications must be on file not later than Sept. 16. *Oral.* Chicago, Dec. 6-7. Applications for Group A must be on file not later than Nov. 1. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* October 21. Applications must be on file not later than September 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 18-19. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Cleveland, Oct. 5. *Written.* Various centers, March 8. *The only written examination during 1941.* Applications must be on file not later than Dec. 1. A special oral and clinical examination will be held on the Pacific Coast during 1941 providing there will be enough candidates to warrant it. Applications for this examination should be on file not later than Sept. 15. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and written.* New Orleans, January 1941. Final date for filing application is November 15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: Memphis, Tenn., Nov. 17, preceding the annual meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, December 18-19. Final date for filing application is October 8. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Boston, Sept. 26-29. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Part I. Various centers, October 21. Final date for filing application is September 15. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Oral and Written.* Chicago, February 1941. Applications must be on file not later than Oct. 15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

California Reciprocity Report

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports sixty-six physicians licensed by reciprocity and twelve physicians licensed by endorsement from January 2 through April 26. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Evangelists	(1938)		Colorado, Nebraska
Univ. of California Medical School	(1934)	Kansas, (1936)	Idaho
University of Colorado School of Medicine	(1928)		Colorado
George Washington University School of Medicine	(1934)		Penna.
Georgetown University School of Medicine	(1933)		Maryland
Emory University School of Medicine	(1935)		Georgia
Bennett College of Eclectic Med. and Surgery, Chicago	(1911)		S. Dakota
Chicago College of Med. and Surgery	(1912)	Illinois, (1914)	S. Dakota
College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois	(1909)		Illinois
Northwestern University Medical School	(1908), (1932), (1936), (1938)		Illinois
Rush Medical College	(1935)	Colorado, (1936)	Minnesota
The School of Medicine of the Division of Biological Sciences	(1934)		Minnesota
Univ. of Illinois College of Medicine	(1935)	Missouri, (1936)	Illinois
Indiana Univ. School of Med.	(1925), (1929), (1934), (1938)		Indiana
State University of Iowa College of Medicine	(1930)		Iowa
University of Kansas School of Medicine	(1936), (1938)		Kansas
Johns Hopkins University School of Medicine	(1935)		Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons	(1935, 2)		Utah
University of Minnesota Medical School	(1914), (1924), (1925), (1936)		Minnesota
St. Louis University School of Medicine	(1938)		Missouri
Washington University School of Medicine	(1929), (1931)		Missouri
Creighton Univ. School of Medicine	(1933)	Iowa, (1936)	Washington
Lincoln Medical College of Cotner University	(1897)		Colorado
University of Nebraska College of Medicine	(1929)		Kansas, (1937) Nebraska
Columbia University College of Physicians and Surgeons	(1923), (1932), (1933)	New York, (1934)	Minnesota
New York Homeopathic Medical College and Hospital	(1924)		New York
Ohio State University College of Medicine	(1921), (1925)		Ohio
University of Cincinnati College of Medicine	(1936)		Ohio
Western Reserve University School of Medicine	(1932)	(1935) Arizona, (1936) Alabama	Ohio,
University of Oklahoma School of Medicine	(1936)		Oregon
University of Oregon Medical School	(1925), (1938)		Oregon
Hahnemann Med. College and Hospital of Philadelphia	(1934)		Delaware
University of Pennsylvania School of Medicine	(1926)		New York
Woman's Medical College of Pennsylvania	(1924)		Ohio
Vanderbilt University School of Medicine	(1926), (1936)		Tennessee
University of Manitoba Faculty of Medicine	(1925)		Illinois
Western University Faculty of Medicine	(1897)		N. Dakota
Deutsche Universität Medizinische Fakultät, Prag	(1924)		Massachusetts
Magyar Királyi Erzsébet Tudományegyetem Orvostudományi, Pecs	(1926)		Ohio

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists	(1929),	(1932)	N. B. M. Ex.
University of California Medical School	(1939)		U.S.P.H.S.
George Washington University School of Medicine	(1920)		U. S. Navy
University of Michigan Medical School	(1936)		U.S.P.H.S.
University of Minnesota Medical School	(1915)	(1931), (1935)	U. S. Army, N. B. M. Ex.
Cornell University Medical College	(1928)		N. B. M. Ex.
University and Bellevue Hospital Medical College	(1929)		N. B. M. Ex.
Duke University School of Medicine	(1934)		N. B. M. Ex.
Jefferson Medical College of Philadelphia	(1924)		U. S. Navy

Book Notices

Treatment of Cancer and Allied Diseases. By One Hundred and Forty-Seven International Authors. Edited by George T. Pack, B.Sc., M.D., F.A.C.S., Attending Surgeon, Memorial Hospital, New York, and Edward M. Livingston, B.Sc., M.D., Associate Visiting Surgeon, Bellevue Hospital, New York. In three volumes. Cloth. Price, $36. Pp. 920; 923-1812; 1815-2598, with 1,500 illustrations. New York & London: Paul B. Hoeber, Inc., 1940.

The object of these large volumes is to assemble in harmonious correlation the widely scattered information about the methods of treating all stages of all kinds of cancer. The editors were impressed particularly with the need of competent and comprehensive presentation of relative values of surgery and irradiation in cancer. It is a remarkable achievement to have brought together and integrated the contributions of 147 leaders in the practical treatment of the cancerous diseases. Of the 147 authors, eleven are European. The vast scope of the volumes is best shown by listing the main topics considered: general principles of treatment, cancer of the mouth and pharynx, larynx, neck, thyroid and parathyroid, breast, chest, esophagus, stomach, intestinal tract (including gallbladder, liver, pancreas, spleen, mesentery, retroperitoneal space), colon, rectum, female genitals, urinary system, male genitals, skin, eye and orbit, nervous system, bone and synovial membranes, lymphoid system, and finally miscellaneous topics (electrosurgery, emergency ligations, rectal anesthesia, fever and lead treatments, care of incurable and terminal cases, nursing in cancer). It is out of the question to comment on single articles and no attention can be given to the way in which the various authors handle their subjects. The articles vary in length from three or four pages to monographic presentations. Many articles have been published elsewhere, notably the overwritten monograph by the editors on the results of the surgical treatment of gastric cancer (Livingston, E. M., and Pack, G. M.: End Results in the Treatment of Gastric Cancer: An Analytical Study and Statistical Survey of Sixty Years of Surgical Treatment, New York, Paul B. Hoeber, Inc., 1939; 153 pages with 356 references). The illustrations, all black and white, are uniformly of excellent quality. Many of them are reproductions by the courtesy of publishers of books and periodicals. There are many elaborate and complicated charts and tables, some of which are not easily understood.

Volumes 1 and 2 have separate indexes; at the end of the third volume is the complete subject index for all three volumes. The pages in each volume are given on the backbone. There is no author index. The paper is heavily calendered. Each volume weighs about 6½ pounds. The spacing between the subsections of the text is unusually wide. This is true also of certain tables and especially of prescriptions. The prescriptions for the treatment of incurable cancer on pages 2571-2593 could easily have been printed clearly on half a dozen pages or so. The publishers evidently like wide open spaces. Why overdo? The general typography is of standard excellence, but the section and chapter titles are printed in such large type that one is reminded of newspaper headlines.

Painstaking work by the editors is evident throughout. While each author as a matter of course is responsible for his statements, the editorial supervision has secured a good degree of uniformity of presentation. Uniformity of nomenclature could hardly be expected, however. In the case of some of the contributors there may be a tendency perhaps to rely too absolutely on microscopic structure as a criterion of the radioresistance of certain cancers. All references have been verified. In most cases the references contain the titles of articles in periodicals. The question arises whether such titles are of value enough to justify the labor and space required to print them.

The editors have written valuable introductions to certain sections, e. g. cancer of the breast, esophagus and rectum, and also instructive comments in many places. Special stress has been placed on giving the end results obtained with various forms of treatment.

Enough has been said to make it plain that a contribution of great service has been made to the literature of cancer. An immense storehouse of information and guidance has been provided for all who take direct part in the immediate, practical treatment of the cancerous diseases.

¿Por qué es necesario conocer la historia de un mensaje a García? (Anotaciones para fijar la técnica del Servicio de salubridad de un Terremoto). Por el Dr. Victor Grossi G. (Publicado en la Revista asistencia social). Paper. Pp. 174, with illustrations. Valparaiso, Chile: The Author, 1939.

One shot fired in New England was heard round the world. The message sent by the armed forces of the United States to the Cuban leader of the Spanish-American War of 1898 and immortalized by Hubbard is now being repeated in South America. Army leaders in Russia and Japan have resorted to it as an inspiration to their men. The present author has used it as title and introduction to his description of the work accomplished by the health authorities of Chile in the emergency created by the earthquake that devastated the southern part of the country in January 1939. A number of towns were in ruins and about 30,000 persons had been killed. Sanitation was the most urgent matter, since the deaths exceeded the injured, and the immediate needs were safe water, shelter and protection against disease. One day after the earthquake, physicians and health workers were already on duty furnishing all medical or sanitary relief required by the circumstances. One of the sanitary engineers of the Pan American Sanitary Bureau also arrived and took charge of the water supply problem. In describing in detail the work accomplished, Dr. Grossi, one of the leading participants in the rescue, also emphasizes the need to be prepared for similar disasters in the future and ends with a tribute to the medical profession. In 1939, as previously in 1906, physicians rallied to the call of duty, performed without hesitation the work expected of them, and fulfilled every hope, rising indeed to the needs of the occasion.

The 1939 Year Book of Physical Therapy. Edited by Richard Kovács, M.D., Clinical Professor and Director of Physical Therapy, New York Polyclinic Medical School and Hospital, New York. Cloth. Price, $2.50. Pp. 472, with 155 illustrations. Chicago: Year Book Publishers Incorporated, 1939.

This is the second yearbook on physical therapy that has been published, and the excellent standard set last year has been maintained in the present edition. The book is divided into two parts. The first part deals with methods of physical therapy and the second with applied physical therapy. The first part is subdivided into sections on general considerations, thermotherapy, fever therapy, electrotherapy, electrosurgery, ultra sound waves, light therapy, hydrotherapy, balneotherapy and climatotherapy, mechanotherapy, occupational therapy and institutional work. The second part is subdivided into sections on general considerations, peripheral vascular diseases, infantile paralysis, pulmonary, abdominal, miscellaneous medical, arthritic and rheumatoid conditions, as well as traumatic and orthopedic, neurologic and mental, pediatric, gynecologic and genito-urinary conditions, including syphilis and gonorrhea. Proctologic, dermatologic and ophthalmologic diseases and also conditions of the ear, nose and throat are considered. The abstracts of material in many foreign languages make this book a noteworthy contribution on contemporary physical medicine. The careful classification of material makes it an excellent reference work for any one who is desirous of obtaining the latest information concerning the various phases of this important subject. The generous use of illustrations is to be commended and the editor is to be complimented on another extremely interesting edition of this yearbook, which is recommended not only to every physician interested in physical therapy but also to general practitioners and specialists in other fields.

Historia da lepra em S. Paulo. Pelo Flavio Maurano. Volumes I e II. (3.ª Monografia dos Arquivos do Sanatorio Padre Bento). Paper. Pp. 270, with 26 illustrations; 281, with 127 illustrations. S. Paulo: Emprêsa gráfica da "Revista dos Tribunais," 1939.

The history of leprosy in Brazil may roughly be divided into several chapters. One of the most important is that concerning one of the principal geographic and political divisions of the country: the state of São Paulo. Of the ten chapters in this interesting work, the first two deal with the origin and introduction of leprosy in Brazil and the spread of the disease in Brazilian territory, especially in the state of São Paulo itself, as far back as the eighteenth century and probably long before, with the arrival of Portuguese settlers and especially African slaves. The third is a history of the official action undertaken by various administrations, with the work of the present government being treated in the two final chapters (IX and X). A deserved tribute is here paid to such pioneers as Magalhães, Ribas and Lindenberg, who realized the importance of this question when few indeed even suspected its far reaching scope. Chapter IV describes the lives and history of patients. In chapter V (one of the most interesting parts of Dr. Maurano's book) are discussed scientific concepts and popular beliefs, stress being laid on old confusion as to diagnosis, vogue of certain cures pushed by quacks, and finally the modern scientific period with its many Brazilian contributions. Three chapters (VI, VII and VIII) are devoted to civic cooperation in the care of lepers in former times. This book contains information unobtainable elsewhere, which will be received with appreciation by all interested in public health problems of the Americas, among which leprosy stands out. The number of lepers in the state of São Paulo is estimated at more than 15,000. A number of illustrations, including maps, permit a better visualization of many of the points here emphasized. An idea of the magnitude of the task accomplished so far may be gathered from the fact that the number of patients isolated under controlled conditions has increased from less than 500 in 1928 to more than 7,000 in 1938.

The Chemical Composition of Foods. By R. A. McCance and E. M. Widdowson. Medical Research Council, Special Report Series, No. 235. Cloth. Price, $1.20; 4s. Pp. 150. New York: British Library of Information; London: His Majesty's Stationery Office, 1940.

As a basis for the nutritional and dietetic management of persons with various diseases, it is necessary first of all to have accurate information about the chemical composition of foods. The first comprehensive treatises on the composition of human foods were those of Atwater, published under the auspices of the U. S. Department of Agriculture. Not many investigators have been content to undertake the arduous task of compiling data on foods. It is therefore fitting that Dr. McCance, the senior author, who wished to undertake this project, was granted assistance by the Medical Research Council of Great Britain. The book provides the analytic data which the authors have obtained over a period of many years. There are data on the technic of determinations, notes on the chemical composition of cooked dishes containing several ingredients, with their recipes, and then the tables themselves. The latter, which make up the bulk of the volume, are arranged so as to provide the composition of foods on the basis of 100 Gm. and again in terms of the ounce. The tables provide not only the usual data to be found in most food tables but also data on the available carbohydrate, the anionogen-cationogen value, and data for all the important ash constituents, including sodium, potassium, calcium, magnesium, phosphorus, sulfur, chlorine, iron and copper. Brief supplementary tables provide some data on the so-called available or nonphytin phosphorus in foods and on the percentage of ionogenic iron. There is a suitable index. The foods in the table are divided into cereals and cereal foods (thirty-nine products), dairy products (twenty-two), meat, poultry and game (eighty-two products), fish (eighty-nine products), fruit (seventy-seven products), nuts (ten products), vegetables (sixty-five products),

sugar, preserves and sweetmeats (nineteen products), beverages (sixteen products), beers (six products), condiments (eight products), vegetable fats (two products), cakes and pastries (twenty-eight products), puddings (thirty-six products), meat and fish dishes (thirteen products), egg and cheese dishes (eight products), sauces and soups (ten products). It is apparent that analyses of a great many meats and fish have been made and the data are here made available, frequently for the first time. Among the interesting dishes for which analytic information is made available are bickiepegs, toad-in-the hole, kedgeree, treacle tart, rock buns, lemon curd tarts and cob nuts. This is the kind of information people interested in foods need to know. While the examples mentioned represent British foods, there are many items of more general use for which data are offered.

Nelson Loose-Leaf Specialties in Medical Practice. Edited by Edgar Van Nuys Allen, M.D., Chief of a Section in the Division of Medicine, The Mayo Clinic, Rochester, Minnesota. With a foreword by Donald C. Balfour, M.D., F.A.C.S., F.R.C.S., Consultant in Surgery, The Mayo Clinic. Volumes I and II. Cloth. Price, $25 per set. Pp. 441; 443-934, with illustrations. New York & Edinburgh: Thomas Nelson & Sons, 1940.

Supplementing the other well known loose leaf systems in the field of medicine published by the Nelson Company comes a new series to be known as Specialties in Medical Practice, edited by Edgar Van Nuys Allen of the Mayo Clinic. The contributors in charge of the various sections are all persons of note in the fields concerned, although in many instances associates and assistants in professorships have been chosen rather than the professors themselves, perhaps because most of these names have already been associated with other volumes. What each of the authors does essentially is to write specifically for general practitioners the information that they should have available regarding various medical specialties. This is done, moreover, in exceedingly brief form, which makes the material much more useful for ready reference than the large volumes now available in most medical fields. One of the best chapters is the section on allergy by F. A. Simon, since this field is so rapidly advancing that one finds it difficult to keep abreast of current literature. Also important is the section on endocrinology. The volume is published in loose leaf form, so that subscribers will no doubt be provided with new pages from time to time as additional information is assembled.

Albert Calmette: Sa vie, son œuvre scientifique. Par P. Noël Bernard et Léopold Nègre. Préface de Pasteur Vallery-Radot. Avant-propos de A. Yersin. Paper. Price, $1.15. Pp. 271, with portrait. Paris: Masson & Cie, 1939.

The first part traces the course of events in the life of Calmette. He was born in 1863, was promoted "aide-medicin" at the medical school in Brest in 1883 and served as naval medical officer in the Far East, returning to France in 1887. He became interested in the new science of microbiology, subscribed as one of the first to the *Annales de l'Institut de Pasteur,* took part in a course under Roux and met Pasteur himself, through whose influence he was sent in 1890 to Indo-China to establish the first colonial microbiologic laboratory at Saigon. Here he prepared vaccines, worked on fermentations, began his investigations of venoms, which he continued under Roux in Paris after his return to France in 1893, and in 1895 he was appointed director of the Pasteur Institute at Lille, where he remained until 1919, carrying on his practical and investigative work as best he could during the German occupation of Lille from 1914 to Nov. 11, 1918. Here he began the comprehensive work on tuberculosis in all its phases that eventually culminated in the introduction of BCG as an antituberculosis vaccine. In 1919 Calmette was appointed subdirector of the Pasteur Institute in Paris, where in addition to his administrative duties he established new laboratories for the investigation of the prevention of tuberculosis and the production of BCG on a large scale with control of the results of its use. He died in 1933. The many and diverse details of the remarkable career thus outlined in brief fill four interesting, well organized and well documented chapters. The conditions and influences under which Calmette worked are clearly described. His great ability, devotion to service and good will strongly impress the reader. The second part reviews the scientific work of Calmette under the headings of venoms and antivenom serotherapy, hygienic researches, tuberculosis and BCG vaccination, followed by a chapter on developments since 1933. No undue claims are advanced. It is affirmed that BCG is harmless and that the accumulating facts indicate its value. Calmette himself said in effect that only the future can determine what the social benefits from BCG will be. At the end are listed Calmette's publications according to subjects. The book is a notable addition to the biographies of men of science. It is a worthy record of the achievements and personality of a faithful worker in the school of Pasteur.

Shock: Blood Studies as a Guide to Therapy. By John Scudder, M.D., Med.Sc.D., F.A.C.S., from the Surgical Pathology Laboratory of the College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $5.50. Pp. 315, with 60 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1940.

The elaborate format of this book seems disproportionate to its content. Parsimonious economy of space alternates with profligate waste of it. A historical summary and review of all preceding work on shock is compressed into eight pages, in which 280 references are cited. Toxemia as a cause for shock is presented and refuted in thirty lines. Citations of authors are substituted for analysis of evidence. Sixteen pages is devoted to potassium and four to all other chemical variations. Stripped of titles, tabulations and figures, the textual matter in parts I and II would fill about forty-five pages, 7 inches to the page. This portion contains 103 full page diagrams, figures, graphs or tabulated case histories in minute detail, twenty-one part page figures or tables, and twenty-one blank pages for readers' notes. In part III, thirty-eight pages is used for listing authors chronologically with a line or two summarizing the contribution: "Dale, 1910, Histamine the cause of shock"; "Cannon, 1917, Reduction of alkaline reserve in shock." The reader receives no aid in evaluating and correlating these fragments. The remainder of the book, pages 237-315, consists of bibliography and index.

The origin and mechanism of shock are not discussed coherently. Isolated statements indicate that the author does not support either of the current hypotheses. A new conception, based on chemical alterations of the blood with vasoconstriction as a fundamental factor, is suggested. No attempt is made to correlate this idea with known physiologic reactions or with the pathology of shock. Hemoconcentration, shown by specific gravity, is emphasized as an early sign, but its possible relation to endothelial permeability is not mentioned. "Changes in the specific gravity of the blood measure changes in vasoconstriction." Hyperpotassemia is explained as indicating profound cellular injury. The data show that hemoconcentration precedes the hyperpotassemia. This fact would indicate that the latter is a secondary feature rather than a prime causative factor. Valuable practical features of this book are hemoconcentration as an early sign and the author's experiences in treatment. A reader seeking information concerning the origin and nature of shock will be disappointed.

Experimentelle Untersuchungen über die spontanen Veränderungen des Blutes in Vitro. Hinsichtlich Suspensionsstabilität, Komplementaktivität, und Antithrombinfunktion. Von Bengt Bergenhem. Acta pathologica et microbiologica Scandinavica Supplementum XXXIX. Paper. Pp. 251, with 50 illustrations. Uppsala: Almqvist & Wiksells Boktryckeri-A. B., 1938.

This monograph is divided into three major sections: (1) suspension stability of red blood cells, (2) complement activity and (3) antithrombin function. The introductory remarks are devoted to the earlier work of Fahræus and the author on the suspension stability of red blood cells. The main purpose of the present investigation was to study further the "stabilisierende substanz" which is adsorbed by red cells when serum or plasma is heated to body temperature and thus inhibits the aggregation tendency. This substance is considered identical with lysolecithen. Chapter I is devoted to the historical background of the problem. Chapter II deals with material and methods. In this section the author discusses the influence of defibrination and substances which prevent coagulation on the stabilization process, the morphologic changes of the red cells, the stabilizing process in serum and plasma, the stabilization process and splenic function, and the loss of the stabilizing process in serum and plasma through shaking. Chapter III considers the relation of complement to the stabilization process. Chapter IV deals with the coagulation process, the parallel between the destruction of the red cell aggregation and coagu-

lation enhancing properties of the serum, and antithrombin function of the serum. The author concludes that, with increasing temperature, coagulation activity is paralleled with the decrease of the erythrocyte aggregation. Chapter v includes discussions on saponin hemolysis and the action of tetanotoxin on red cell hemolysis. Finally, the author summarizes his data contained in all the preceding chapters. The work is highly theoretical but should be of provocative interest to hematologists and those interested in hemolysis and hemoagglutination.

Gardiner's Handbook of Skin Diseases. Revised by John Kinnear, T.D., M.D., M.R.C.P., Physician for Diseases of the Skin, Dundee Royal Infirmary, Dundee. Fourth edition. Cloth. Price, $3.50. Pp. 239, with 70 illustrations and 16 colored plates. Baltimore: William Wood & Company, 1939.

In this revision the aim has been to provide a hand book for the general practitioner and medical student and to give an adequate description of the common diseases of the skin with brief reference to the rarer disorders. Only those measures which have proved useful in routine practice are discussed under treatment. The illustrations are good. The material of the book is well classified in the table of contents. The chapter on toxic dermatoses is well done and contains a good discussion of the subject of "sensitization." Sulfanilamide is briefly discussed in the treatment of pemphigus. This brief textbook is good and should adequately serve its purpose as a "hand book for the general practitioner and medical student."

The British Encyclopaedia of Medical Practice Including Medicine, Surgery, Obstetrics, Gynaecology and Other Special Subjects. Surveys and Abstracts 1939. Cumulative Supplement 1939. Under the General Editorship of Sir Humphry Rolleston, Bt., G.C.V.O., M.D. Publishing Editor: Adam Clark, L.M.S.S.A. Sub-Editor: G. Faulkner, D.Sc. Cloth; Boards. Price, $9. Pp. 605, with 33 illustrations; 170. Toronto & London: Butterworth & Co., Ltd., 1940.

Supplementary to the British Encyclopaedia of Medical Practice, which has been regularly reviewed in these columns, comes a new volume of Surveys and Abstracts and another volume called Cumulative Supplement. The Critical Surveys include authoritative reviews of certain branches of medical science, particularly one on the state and national health by Sir Arthur MacNalty, chief medical officer of the Ministry of Health, London. Others concern general surgery, pediatrics, diseases of the blood-forming organs and other special medical fields. Following the Critical Surveys are discussions of advances in the field of drug therapy, and finally at least half of the volume is devoted to abstracts of medical literature. The price of the volume being considerable, one questions its desirability as a permanent addition to a library, since much of the material it contains is obviously ephemeral. In order to keep The British Encyclopaedia of Medical Practice abreast of progress it has been decided to publish an annual supplemental service planned to present new medical information which has become available since the publication of the original work, the idea being that one reads first the articles in the original twelve volumes of the encyclopedia and thereafter follows with the material under the various headings in the Cumulative Supplement. The selection of the abstracts has been excellent, since it might be said that there is hardly one of them which does not provide useful information.

Manual of Dermatology. By Carroll S. Wright, B.S., M.D., Professor of Dermatology and Syphilology, Temple University School of Medicine, Philadelphia. Cloth. Price, $4. Pp. 376, with 138 illustrations. Philadelphia: Blakiston Company, 1940.

This manual was written chiefly for medical students and general practitioners of medicine. The illustrations have been excellently reproduced on good paper by the publishers, and the text is printed in clear legible type. Sulfanilamide, nonspecific protein and vitamin therapy are briefly discussed. Parallel differential diagnostic tables are given in many entities, which should be of great value to one inexperienced in dermatologic diagnosis to help properly classify an entity. The sections on tuberculosis, syphilis and diseases due to vegetable parasites are well done and well illustrated. As a compact volume the book admirably serves its purpose as a small text or reference book to be used in connection with clinic and class work and to be complemented by the larger textbooks when more lengthy discussions of a cutaneous entity or bibliography is desired.

Miscellany

TOTAL OF SUICIDES IN THE UNITED STATES EXCEEDS 300,000 FOR 1920-1938

Suicides in the United States totaled more than 300,000 during nearly two decades covered in a report for the years 1920 to 1938 inclusive just issued by the Division of Vital Statistics in the U. S. Bureau of the Census. The exact total was 300,580 suicidal deaths.

The death rate for suicides ranged from 10.2 per hundred thousand of estimated population in 1920, the first year covered in the report, to 15.2 per hundred thousand of estimated population in 1938. The rate for 1938 was the highest since the heavy depression period of 1930 to 1933 inclusive. The highest rate for all years covered in the report was 17.4 in 1932. The next highest rate was in 1931 with 16.8. The rate for 1933 was 15.9 and for 1930 it was 15.7.

Deaths by Suicide and the Rate per Hundred Thousand of Estimated Population in 1938

Area	Number	Rate
Registration area	19,802	15.2
Alabama	220	7.6
Arizona	89	21.6
Arkansas	174	8.5
California	1,874	30.5
Colorado	206	19.2
Connecticut	272	15.6
Delaware	44	16.9
District of Columbia	143	22.8
Florida	264	15.8
Georgia	305	9.9
Idaho	97	19.7
Illinois	1,271	16.1
Indiana	594	17.1
Iowa	418	16.4
Kansas	292	15.7
Kentucky	309	10.6
Louisiana	179	8.4
Maine	152	17.8
Maryland	276	16.4
Massachusetts	590	13.3
Michigan	730	15.1
Minnesota	420	15.8
Mississippi	147	7.3
Missouri	633	15.9
Montana	103	19.1
Nebraska	236	17.3
Nevada	36	35.6
New Hampshire	94	18.4
New Jersey	696	16.0
New Mexico	47	11.1
New York	2,248	17.3
North Carolina	336	9.6
North Dakota	75	10.6
Ohio	1,274	18.9
Oklahoma	258	10.1
Oregon	221	21.5
Pennsylvania	1,397	13.7
Rhode Island	73	10.7
South Carolina	126	6.7
South Dakota	74	10.7
Tennessee	317	11.0
Texas	728	11.8
Utah	63	12.1
Vermont	59	15.4
Virginia	378	14.0
Washington	444	26.8
West Virginia	247	13.2
Wisconsin	527	18.0
Wyoming	46	19.6

Of the states, Nevada reported the highest suicide rate per hundred thousand of estimated population in 1938 with 35.6; South Carolina reported the lowest rate with 6.7. In total number of suicides in 1938, New York led all the states with 2,248, while Nevada reported the smallest number with thirty-six suicides. California ranked second in total number of suicides in 1938 with 1,874, Pennsylvania third with 1,397, Ohio fourth with 1,274 and Illinois fifth with 1,271 suicidal deaths.

Death totals by suicide and the rate per hundred thousand of estimated population for the forty-eight states and the District of Columbia 1938 are given in the table.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Act: Melanoma Resulting from Mole Irritated by Sand and Ashes an Accidental Injury.—In the course of his employment the workman for a period of about one month operated a machine which made building blocks from ashes, sand and cement. Some sand and ashes invariably fell into his shoes. While at work on July 15, 1936, he felt a severe pain at the site of a pigmented mole, about one half inch (1.25 cm.) in diameter, which he had on "the outer aspect of his instep, just above the little toe" of his left foot. Later that afternoon he noticed that his left sock was stained with blood and that the mole appeared to have been scratched "like the ashes irritated it a little bit." The mole was sore and caused him to limp somewhat, but he continued to work. About four weeks later, some time in August, the mole began to "ooze" and, on the advice of the physician whom he consulted, he was hospitalized for three days. It was discovered that the mole had developed into a malignant tumor, a melanoma, and it was "surgically removed." Six weeks later he was again hospitalized and, because of objective evidence that the disease had spread, "another operation was performed upon the foot and leg as far as the groin." He was released from the hospital thirty-eight days later. He returned to work in January 1937 and was assigned light work. He was denied compensation under the workmen's compensation act of New Jersey by a referee of the workmen's compensation bureau and he appealed to the courts, the case ultimately reaching the Court of Errors and Appeals of New Jersey. Pending the appeal the workman died, presumably from the melanoma.

Compensation was denied the workman by the workmen's compensation bureau and by the lower courts on the theory that since the workman's ailment arose from a "constant irritation of the mole" it was an occupational disease and as such was not compensable under the New Jersey workmen's compensation act, which provides compensation only for a personal injury by accident arising out of and in the course of employment. The Court of Errors and Appeals, however, could find in the record no evidence that there was "constant irritation of the mole" prior to July 15, 1936, nor could it agree with the conclusion of the workmen's compensation bureau and of the lower courts that the testimony did not establish "accidental injury at any time." In the judgment of the court, the evidence did establish (1) that the claimant obviously suffered injury on July 15, which was manifested by pain, limping, bleeding of the mole and the scratch which appeared thereon and (2) that sand and ashes were present around the mole when the injury occurred. The impinging of the sand and ashes on the mole constituted, as all of the medical witnesses agreed, the application of traumatic force, if in the instant case that element is necessary to make out an injury by accident under the workmen's compensation act. While there may have been continued irritation of the mole from July 15, the date when the workman was first injured, to the time in August when he consulted a physician, that did not make the injury any less a compensable injury. If, for example, at a given time sand had struck and lacerated the cornea of the workman's eye, no one would contend that it was not an accidental injury even though previously sand had daily gotten into his eye but had done no damage other than to collect around the margins of the eyelids. In principle there is no defensible distinction between this supposititious case and the instant one.

An injury or death, said the court, to be compensable under the workmen's compensation act must have arisen from accident out of and in the course of employment. Here admittedly the injury arose out of and in the course of the employment, but was there an accidental injury? To be compensable it is not necessary that an accidental injury be the result of traumatic force. The fact that the injury was accidental may legitimately be inferred from circumstantial evidence. An accident is "an unlooked-for mishap or untoward event which is not expected or designed" or "an unintended or unexpected occurrence which produces hurt or loss." It is clear that the term "accident" is used in the act, and should be so considered, in its ordinary, popular and accepted sense. An "accident," therefore, need not be due to any extraneous event or occurrence. Reverting to the testimony, said the court, there was no claim by the employer that "cancer" was already present at the time of the injury on July 15, or that "cancer" would have resulted in any event apart from employment. There was ample testimony of an unexpected occurrence resulting in an injury on July 15. Furthermore, there was an undisputed causal connection between the injury of July 15 and the fatal result. Also no proof was advanced that the mole was ever irritated before the date in question. The medical testimony showed that the impinging of the sand on the mole and the irritation caused thereby on July 15 produced the melanoma. Accordingly, the court held that the disability and resulting death of the workman was the result of an accidental injury and that the workman's widow was entitled to compensation.—*Bollinger v. Wagaraw Bldg. Supply Co. (N. J.), 6 A. (2d) 396.*

Lead Poisoning Following Short Exposure to Paint Spray Not an Accidental Injury.—Bailey, in the course of his employment as a laborer for Salt Lake City, started, March 24, 1935, painting trucks with a paint spray. No mask was furnished him. He became ill April 10 and died April 15 from lead poisoning, allegedly resulting from inhalation of the vaporized paint. The industrial commission of Utah denied his mother, the plaintiff, compensation under the Utah workmen's compensation act on the ground that the workman's illness was an occupational disease and was not compensable under the Utah act, which provides compensation only for injury or death "by accident arising out of or in the course of" employment. Subsequently the mother brought suit against the city under the so-called wrongful death statute, which authorizes an action against a tort feasor "Except as provided in [the workmen's compensation act] . . . when the death of a person . . . is caused by the wrongful act or neglect of another . . ." The trial court sustained a demurrer interposed by the city on the assumption that the action was barred by the workmen's compensation act. The plaintiff then appealed to the Supreme Court of Utah.

The main question to be determined by the Supreme Court was whether Bailey's ailment was an occupational disease or an accidental injury, for the court assumed that if the workman had contracted an occupational disease the action of the trial court was in error and that if the workman's ailment was an accidental injury the ruling was correct. The court then considered cases holding that where injury is traceable to a particular time, place and circumstance it is an accidental injury but where the condition arose gradually and cumulatively from the character of the employee's work it is an occupational disease. If the illness, said the court, is one commonly recognized as incident to the particular occupation, it is an occupational disease. The time taken for the effects of the occupation to become serious is not the governing factor. Some people are less resistant to imperfect conditions than others. To stress length of time as a basis of determining the accidental nature of an illness is to adopt a rule which may, in many cases, be governed by the person's bodily resistance. If such a rule were adopted, the dividing line between an occupational disease and an accidental injury would become extremely hazy as the periods of time for each approached unity. The fact that the workman in this case succumbed in a comparatively short time to lead poisoning from inhaling the vapor was not conclusive that his illness was accidental.

In deciding a case of this kind, continued the court, we should ascertain first whether the illness is one commonly recognized as incident to the usual performance of the occupation. If it is not, then the question of an occupational disease is ended. If it is incident to such performance, then we should ascertain whether some definite unexpected or unusual circumstance took place—something that interjected itself into the usual course of the performance of the occupation. And, finally, we should ascertain whether or not this circumstance, if one there be, accelerated or changed the effect of the otherwise resultant occupational illness. If it did, then that illness was the result of an accidental injury. But, from the fact that an unexpected

or unusual circumstance may accelerate an illness, we must not reason backward and say that the shortness of the period of exposure to imperfect conditions of employment before an illness develops proves that there was some unusual circumstance about the performance of the occupation that made it accidental. The result must be traceable to a particular circumstance, which should be identified as to time and place and not merely inferred. In the instant case the workman suffered an illness which he did not know might follow from breathing the vaporized paint. So far as the records showed, no circumstance occurred in the performance of his employment which differed from the usual performance of such labor of painting with a spray gun. The city's failure to give him a mask, whether deliberate or through carelessness, was not accidental. The unusual or unexpected circumstance which classifies an illness as accidental must occur in the events leading up to the illness. From the fact that Bailey did not know what would be the effects on his health of the performance of his employment, we must not conclude, said the court, that his resultant illness, which to others with superior knowledge would be an occupational disease, was an accidental injury. Lack of knowledge of results is not the circumstance to which the illness must be traceable. That circumstance must lie in the causal connection between the occupation and the illness.

The Supreme Court held, therefore, that action under the wrongful death statute was maintainable, since Bailey's injury and death were not compensable under the workmen's compensation act. Accordingly, the judgment of the lower court sustaining the demurrer and dismissing the action was set aside and the case remanded.—*Young v. Salt Lake City (Utah), 90 P. (2d) 174.*

Optometry Practice Act: Legality of Corporate Practice; Optometry Not a Learned Profession.—Lansburgh and Bro., a corporation operating a department store in Washington, D. C., leased space in the store to the Buhl Optical Company, a corporation, in which to conduct a so-called optical department for the examination of eyes and the sale of eyeglasses and other optical goods. The optical company agreed to pay as rent a sum equal to 20 per cent of the gross volume of business done therein and to spend a sum equal to at least 5 per cent for advertising. The department store agreed to collect and pay over to the optical company all receipts from credit sales made in the "optical department" after deducting the rent and the salaries of the employees in that department. Although these employees were paid by the department store, they were hired by the optical company, were subject to its exclusive control and were not subject to the direction or supervision of the department store. The "optical department" was placed in charge of an optometrist, duly licensed in the District of Columbia, who was employed on a salary basis and paid by the department store.

The plaintiffs, licensed optometrists, brought suit in the district court of the United States for the District of Columbia to enjoin the department store and the optical company, the defendants, from engaging in the practice of optometry. The plaintiffs alleged (1) that optometry is a learned profession and its very nature prohibits a practitioner thereof "from any affiliation or connection with a corporation or non-optometrist" and (2) that the optometry practice act of the District of Columbia specifically prohibits the employment of duly licensed optometrists by a corporation or non-optometrist. The district court, however, held that optometry is not a learned profession comparable with law, medicine and theology but is in its nature empirical and "essentially a mechanical art which requires skill, manual dexterity, and a knowledge of the use and application of certain mechanical instruments and appliances designed to measure and record the errors and deviations from the normal which may be found in the human eye." The court refused to grant the injunction sought and so the plaintiffs appealed to the United States Court of Appeals for the District of Columbia.

In *United States* v. *American Medical Association* (District of Columbia), 110 F. (2d) 703, said the Court of Appeals, this court pointed out that in the District of Columbia the practice of medicine, which is subject to licensing and regulation, may not lawfully be subjected to commercialization and exploitation, and that a corporation is engaged unlawfully in the practice of medicine when it employs licensed physicians to treat patients, itself receives the fee and has for its main object the profit motive. This rule, however, does not apply to the practice of optometry. Nothwithstanding the fact that the optometry practice act prescribes certain educational and professional qualifications which applicants for licensure must meet, optometry is not "one of the learned professions." In so holding the court quoted with approval from E. E. Arrington's History of Optometry (1929), p. 24:

> Ocular refraction is not, and never has been, a part of medicine, either by inheritance, basic principles, development or practice. It is an applied arm of optical science, resting upon the work and discoveries of physicists and opticians through the ages, down to modern times. It does not treat the eye, whether in health or disease, but adapts the light waves which enter the eye, in accordance with optical principles, so as to produce focused and single vision with the least abnormal exertion on the part of the eye. And, finally, its distinction from and independence of medicine have been affirmed by supreme court decisions in every case in which the question has been brought up for adjudication.

It was the opinion of the court that the optometry practice act neither requires nor contemplates that an optometrist shall be a graduate physician nor that he shall, like an oculist or ophthalmologist, diagnose or treat diseases of the eye. In actual practice, the optometrist only measures the refractional abnormalities of the eye and prescribes and sometimes grinds lenses to correct them. While there are cogent reasons for preventing the practice of law and medicine through corporations, no such reasons are apparent with respect to the practice of optometry. The professional service required of a physician or a lawyer creates a relationship of trust and confidence. The necessary disclosures which the patient or client must reveal to the physician or lawyer create a personal relationship which cannot exist between patient or client and a profit-seeking corporation. The universal recognition of a confidential association between the physician and the lawyer and those who engage their services justifies the rule that their allegiance must be wholeheartedly to the patient or the client and not to another. In the case of optometry, however, while it may be a profession in the colloquial sense of the term, there is no more reason to prohibit a corporation from employing licensed optometrists than to prohibit similar employment of accountants, architects or engineers. Furthermore, the court could find nothing in the optometry practice act itself to prohibit corporations from employing licensed optometrists to perform optometric services. The primary purpose of the act is to insure the rendering of optometric services by competent persons and thus to protect the public from inexpertness. That purpose may be accomplished even though the optometrist is employed by a corporation. For the reasons stated, the Court of Appeals affirmed the judgment of the district court denying injunctive relief.—*Silver v. Lansburgh & Bro. et al. (District of Columbia), 27 F. Supp. 682; 111 F. (2d) 518.*

Society Proceedings

COMING MEETINGS

American Association of Railway Surgeons, Chicago, Sept. 16-18. Dr. Daniel B. Moss, 547 West Jackson Blvd., Chicago, Secretary.
American Congress of Physical Therapy, Cleveland, Sept. 2-6. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.
American Hospital Association, Boston, Sept. 16-20. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.
Colorado State Medical Society, Glenwood Springs, Sept. 11-14. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.
Idaho State Medical Association, Sun Valley, Sept. 11-14. Dr. J. N. Davis, 204 Fourth Ave., East, Twin Falls, Secretary.
Kentucky State Medical Association, Lexington, Sept. 16-19. Dr. A. T. McCormack, 620 South Third St., Louisville, Secretary.
National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
Oregon State Medical Society, Eugene, Sept. 4-7. Dr. Morris L. Bridgeman, 1020 S.W. Taylor St., Portland, Secretary.
Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.
Virginia, Medical Society of, White Sulphur Springs, W. Va., July 29-31. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.
Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.
West Virginia State Medical Association, White Sulphur Springs, July 29-31. Mr. Joe W. Savage, Public Library Bldg., Charleston, Executive Secretary.
Wisconsin, State Medical Society of, Milwaukee, Sept. 18-20. Mr. J. G. Crownhart, 110 East Main St., Madison, Secretary.
Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

199:749-892 (June) 1940

*Antienzymatic Nature of Sulfanilamide's Bacteriostatic Action. R. R. Mellon, A. P. Locke and L. E. Shinn, Pittsburgh.—p. 749.
Effect of Sulfanilamide Compounds on Endocarditis. R. H. Major, Kansas City, Kan.—p. 759.
Sickle Cell Anemia in a White Family. L. Greenwald and J. B. Burrett, New York.—p. 768.
Effect of Storage on Prothrombin Content of Citrated Blood. J. Reinhold, Eleanor H. Valentine and L. K. Ferguson, Philadelphia.—p. 774.
Role of Water Balance in Clinical Manifestations of Allergy. R. A. Kern, Philadelphia.—p. 778.
Electrocardiographic and Serum Potassium Changes in Familial Periodic Paralysis. H. J. Stewart, J. J. Smith and A. T. Milhorat, New York. —p. 789.
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*Incidence of Neuropathy in Pellagra: Effect of Cocarboxylase on Its Neurologic Signs. F. H. Lewy, Philadelphia; T. D. Spies and C. D. Aring, Cincinnati.—p. 840.
Cerebral Carbohydrate Metabolism During Deficiency of Various Members of Vitamin B Complex. H. E. Himwich, Albany, N. Y.; T. D. Spies, Cincinnati; J. F. Fazekas and Sarah Nesin, Albany, N. Y. —p. 849.
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Bacteriostatic Action of Sulfanilamide.—Mellon and his co-workers discuss the amount of hydrogen peroxide per unit of bacterial substance necessary for bacteriostasis in the presence of sulfanilamide and the dependence of bacteriostasis on an adequate supply of oxygen. A progressive decrease in oxygen tension of the cultures is accompanied by a decrease in the bacteriostatic effect caused by sulfanilamide. The fact that such diverse species of bacteria as hemolytic streptococci, pneumococci, gonococci, meningococci and Bacillus coli produce hydrogen peroxide and that they are all rather highly sensitive to its toxic effect offers plausible explanation for the broad therapeutic coverage of the drug. When the hydrogen peroxide-producing power of the pneumococcus is suppressed, it is no longer vulnerable to the drug sulfapyridine. Enzymes other than catalase are affected either directly by the drug or possibly secondarily by the toxic action of accumulated hydrogen peroxide. Peroxydase is adversely affected and certain dehydrogenases are inactivated. Antienzymatic conception is sponsored without, however, limiting the effect to a single enzyme. The conception does not exclude toxin inactivation as supported by Carpenter. Toxins are notoriously susceptible to oxidation. The oxidative-enzymatic theories are rather generally supported by clinical evidence. Virtually all the infections decisively influenced are of aerobic nature. An exception is the staphylococcus. The highly reducing nature of staphylococcic lesions is regarded as preventing the oxidation of sulfanilamide that conditions its antienzymatic effect. Whether this explanation is adequate will perhaps be apparent when more is known of the action of the sulfathiazoles, which appear effective against this organism. It is also possible that the protein degradation products present in abscesses may condition the action of the drug in accordance with mechanisms that are not anaerobic. The decisive action of sulfanilamide against Bacillus coli in urine but not in peptone-containing mediums leaves no doubt of the importance of environmental factors. In fact, they may result in multiplying the effect of the drug many times. This potentiating action is particularly conspicuous when antiserums are combined with the drug. The effect of bacteriostasis against pneumococci in vivo is to bring about their "dissociation" into culture phases, whose principal metabolic functions, including hydrogen peroxide formation and virulence, are so critically suppressed that the organisms fall easy prey to the destructive action of the phagocytes.

Conditioned Reflex for Treatment of Alcoholism.—During the last four years Voegtlin has treated 685 cases of chronic alcoholism by utilizing emetine and apomorphine to elicit the unconditioned reflex of nausea and vomiting. Aversion to alcohol is developed during a number (usually from five to seven) of séances or treatments with rest periods between. No food, except liquids, and no sedative drugs are given for at least twelve hours before each treatment. Alarming though not dangerous collapse may follow the injudicious administration of the medication. The treatment room is soundproofed to avoid extraneous stimuli. The lighting is subdued with the exception of the treatment table with its array of liquors, which is "spot lighted," causing the sight of liquor to become an element of the conditioned stimulus. Similarly, by forcing the patient to smell deeply of various liquors the olfactory sense may also be utilized. Usually this aversion to sight and smell is sufficient to cause the patient to avoid alcohol without the more dangerous experiment of tasting liquor. Since the conditioned stimulus is specific, it is necessary to use every conceivable type of liquor. A fall in systolic blood pressure below 100 is an indication for rest and ephedrine medication until a near normal level is again reached. It is well to mention casually to the patient that the medication (emetine and apomorphine) is merely a stimulant to support him during the ensuing violent nausea and also suggests that the drinking of the liquor causes the acute illness. Experience alone will enable one to judge the exact moment when the emetine nausea will begin (usually from two to eight minutes) and consequently the exact moment when the first drink of liquor should be offered. This first offering of liquor should be given within several seconds of the onset of nausea and it should never be withheld until nausea or salivation has appeared. If an error in timing has been committed, the onset of nausea may be hastened by administering from 1 to 2 grains (0.065 to 0.13 Gm.) of emetine orally in whisky. Following the onset of nausea all types of liquor are forced on the patient, making certain that each empty glass is smelled deeply. Warm water is given frequently in order to afford easy emesis and to avoid retching. After emesis is completed the treatment is repeated until the nauseant effect has begun to wane. The stomach is then thoroughly emptied and washed by means of the Ewald tube with warm water. The patient is left in the treatment room until the pilocarpine diaphoresis has ceased. The stomach must be emptied promptly if a patient is unable to regurgitate. Absorption of alcohol to the point where an effect is noticed by the patient will vitiate the entire treatment. Contraindications to the treatment are the cardiovascular-renal syndrome, hepatic cirrhosis with or without esophageal varices, hernia (unless guarded), active peptic ulcer, recent hematemesis and active psychosis. The exact status of 538 of the patients treated is known. During each six month period for the last four years the proportion of sobriety has been remarkably constant, varying only between 62 and 69 per cent. While the proportion of abstinence for the six months immediately following treatment is 97.3 per cent, the proportion during the second six months is only 65.7 per cent. If a relapse does not occur during the first year, its subsequent occurrence is not great. A conservative expectation of 64.3 per cent of total and permanent cures is obtained from an average of eight six month periods. By a "cure" is meant total and permanent abstinence from alcohol of all types. The percentage of

abstinence among women patients was found to be only 57. Relapses were more common among wine than beer drinkers and least frequent among users of distilled liquors. Many of the patients who have relapsed have presented themselves for retreatment. The prognosis in these patients seems poorer. Delirium tremens developed in only fourteen. Twenty-one patients were admitted in acute delirium. Only one of these thirty-five patients with delirium tremens died. This occurred before treatment was instituted. The mortality of the entire series of cases receiving the complete treatment was a single death (0.14 per cent) due to cardiac failure. Laboratory studies show that while 36.8 per cent of patients had albuminuria on admission only 3.9 per cent did on discharge.

Cocarboxylase for Neuropathy in Pellagra.—Lewy and his associates determined the incidence of neuropathy among fifty pellagrins (thirty female and sixteen male patients between 18 and 66 years of age) and four children between 8 and 13 years of age. More than three fourths of the patients were regarded as having mild or moderately severe pellagra. The preponderance of such cases is explained by the fact that only ambulatory patients were examined. Clinical examination revealed that 75 per cent had polyneuropathy of the motor and sensory nerves, 20 per cent had extrapyramidal signs (one half of these showed mild parkinsonism) and 12.5 per cent had tremor and pyramidal tract signs. Intravenous administration of 50 mg. or more of phosphorylated thiamine (cocarboxylase) to nine of these pellagrins was followed by quantitative improvement in the electrical irritability of a number of muscles of seven of them. Improvement also was observed in the pupillary and corneal reflexes and in the sensitivity to touch and pinprick. These indexes often became normal within one to four hours after injection, and improvement was maintained for from one to five days. The patient then tended to regress and eventually returned to the condition preceding treatment. The clinical effect of cocarboxylase was found to be identical with that of thiamine (vitamin B_1) studied previously. The chemical changes in the blood following administration of cocarboxylase paralleled the clinical neurologic improvement. These observations confirm the premise that the neuropathy which is common among pellagrins is caused by a deficiency of vitamin B_1. Patients who retained most of the injected cocarboxylase improved readily, while those who were unable to retain it showed little or no improvement. The administration of synthetic riboflavin was not followed by a change of the neurologic signs.

American Journal of Physiology, Baltimore

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Effects of Anesthesia on Blood Supply to Hypothalamus. A. E. Laidlaw and Margaret A. Kennard, New Haven, Conn.—p. 650.
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American Journal of Surgery, New York

48:523-720 (June) 1940. **Partial Index**

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Régime for Controlling Pain in Far Advanced Cancer Patients. H. C. Saltzstein, E. H. Lauppe and M. Z. Feldstein, Detroit.—p. 561.
*Diaphragmatic Hernia in Children: Résumé of Sixty-Eight Cases Occurring in Children Under 10 Years of Age Treated by Operation. J. B. Hartzell, Detroit.—p. 582.
Pitfalls of Phrenic Nerve Crushing. W. Stenson, New York.—p. 599.
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Role of Splenectomy in Disorders of Spleen: Report of Series of Thirty-Three Collected Cases. J. R. Phillips, Houston, Texas, and L. F. Knoepp, Beaumont, Texas.—p. 617.
*Treatment of Endocervicitis with Carbon Dioxide Snow (Dry Ice). G. Weitzner, New York.—p. 620.
Transurethral Resection for Cancer of Prostate. C. D. Creevy, Minneapolis.—p. 646.

Diaphragmatic Hernia in Children.—Hartzell reviews sixty-eight cases of diaphragmatic hernia occurring in children 10 years of age or less. There was a total mortality of 32 per cent. Nineteen patients died shortly after operation and are classed as operative deaths. Three died after leaving the hospital, one two months and one six months later, of recurrence which resulted in obstruction. Neither was reoperated on. In the third case the hernia recurred in six months, and the patient died after a second operation. There were two more recurrences. These two patients were operated on again. One made a satisfactory recovery and has remained well. The hernia recurred twice more in the other patient and following the third operation he has remained well. Cyanosis, dyspnea and vomiting are the most common symptoms in children less than 1 year of age, while in older children vomiting, pain and colic are the most common complaints. In children less than 1 year old the dominant symptoms result from cardiac and pulmonary embarrassment, while in older children they result from partial obstruction of the gastrointestinal tract. In any case showing these symptoms, the physical examination may reveal tympany on percussion, dextrocardia, dulness to flatness on percussion and absent or diminished breath sounds on the involved side; râles, diminished excursion on the involved side, retraction of the abdomen, an epigastric mass and a rapid heart beat. No diagnosis can be considered complete without a roentgenogram. In sixty of the sixty-eight cases the x-ray examination was used either to make or to confirm a diagnosis. In five of the eight cases not submitted to x-ray study the diagnosis was definitely missed. The diagnosis of diaphragmatic hernia is more frequently made in the male than in the female, and the operative mortality is higher in the latter. The most common type is the false hernia through the left diaphragm. A diaphragmatic hernia constitutes a menace to life. Except in the case of a symptomless infant less than 1 year of age, a definite diagnosis of a diaphragmatic hernia should be followed by immediate surgical intervention. The abdominal approach is usually the best. No one should favor the combined approach unless necessity demands it. The anesthetist should always be prepared to administer a positive pressure anesthesia if the need arises. Positive pressure anesthesia is indicated in the false hernia in which there is no sac. The truth of this is well verified by the higher mortality in the group operated on via the abdominal approach without the benefit of positive pressure anesthesia. The 7.7 per cent mortality in those operated on by the abdominal route given proper anesthesia is satisfactory. A study of the mortality with relation to the age of the patient reveals that it is definitely higher during the first year of life. The twenty-four cases in the present series occurring under 1 year of age were all congenital, and the mortality was 50 per cent. After the first year the

mortality dropped to 22.7 per cent. In the congenital and acquired cases it was about four times as great as in the traumatic cases.

Solid Carbon Dioxide for Endocervicitis.—Weitzner applied topically a rod of solid carbon dioxide to the cervical canal for from sixty to ninety seconds in the treatment of 325 cases of endocervicitis. The first patient was treated in May 1934 and the last in December 1935; 70 per cent of the patients required only one treatment for a cure (cases with erosion responded more readily to the treatment), 15 per cent required two treatments and 15 per cent were treated three or more times. No postoperative sequelae, such as bleeding, inflammation or stenosis of the cervical canal, have been observed after two and a half years of follow-up. Inspection of the treated areas twenty-four hours after treatment shows them to be covered by a grayish pseudomembrane. Seven days after treatment the areas are no longer so covered. The cervix bleeds readily to touch. Biopsies taken at this stage show areas of necrosis still present, but in general the picture is one of early regeneration, especially in the region of the stratified squamous epithelium. Inflammatory changes are absent. From ten to seventeen days after treatment macroscopic signs of healing are visible. From three to four weeks after treatment the entire area of the erosion is covered by stratified epithelium. Eight weeks after treatment cervical biopsy shows complete cure. In thirty-one of 111 cases atypical cells were found on microscopic study in atypical arrangement, apparently invading the surrounding tissue. These cells resembled the earliest stages of cervical malignant changes to such an extent that treatment was suspended pending further study and follow-up. On the basis of 201 biopsies taken from the cervices showing the atypical cells the following statements are made: 1. There were erosions in all cases prior to treatment. 2. The number of treatments had no influence on the development of atypical cells. 3. The atypism was observed as early as one week after treatment. 4. The duration of the atypism ranged from three months to more than two and a half years. 5. Cases with atypical cells showed macroscopically a perfectly smooth normal cervical surface. Berenblum concluded from his experiments that solid carbon dioxide has no carcinogenic properties either for animals or for human beings. Thus it appears that these nests of atypical cells have nothing in common with true malignant changes. They may be regarded as signs of increased activity of the stratified squamous cell epithelium in a healing erosion.

American Journal of Tropical Medicine, Baltimore

20:345-462 (May) 1940

Discussion of Etiology of Sprue. E. B. Vedder, Washington, D. C.—p. 345.
*Internal Autoinfection in Human Strongyloidiasis. E. C. Faust, New Orleans, and A. de Groat, Little Rock, Ark.—p. 359.
*Treatment of Oxyuriasis. J. S. D'Antoni and W. Sawitz, New Orleans.—p. 377.
The Mosquitoes of Costa Rica. H. W. Kumm, San Jose, Costa Rica, C. A.; W. H. W. Komp and H Ruiz.—p. 385.
Further Observations on Comparative Susceptibility of Nearctic and Neotropical Anophelines to Coindigenous Strains of Plasmodium Falciparum. M. F. Boyd, Tallahassee, Fla., and D. M. Jobbins, Panama City, Republic of Panama.—p. 423.
Study of Winter Activities and Hibernation of Anopheles Quadrimaculatus in the Tennessee Valley. E. H. Hinman and H. S. Hurlbut, Wilson Dam, Ala.—p. 431.
Preservation of Yellow Fever Virus. J. P. Fox and S. Gard, New York.—p. 447.

Internal Autoinfection in Human Strongyloidiasis.—According to Faust and de Groat, critical examination of the parasitologic and clinical literature indicates that hyperinfection (internal autoinfection) is not only a necessary hypothesis to explain the relatively frequent cases of human strongyloidiasis which have persisted for many years in the absence of external sources for reinfection but is supported by experimental, clinical and postmortem evidence. The case reported in this communication provides additional evidence demonstrating a relatively heavy invasion of the deeper layers of the bowel wall and liver by filariform larvae derived from mother worms situated in the overlying mucosa. Except for a localized eosinophilic response around the migrating worms no cellular reaction was provoked by this invasion. This stands in marked contrast to the picture of leukocytosis with hypereosinophilia which characterizes the usual case of acute strongyloidiasis. Self infection in strongyloidiasis may result (1) from the perianal invasion of larvae, (2) from the invasion of the mucosa of the lower levels of the bowel by filariform larvae which have originated from sites of infection at higher levels, (3) from the penetration of filariform larvae into the deeper layers of the bowel at the same level where they were produced in the mucosa or (4) from unmetamorphosed rhabditoid larvae massively penetrating through the muscularis mucosae into the deeper layers of the bowel wall. Probably all persons harboring Strongyloides are potential subjects of self infection. The authors stress that self infection with Strongyloides stercoralis may be controlled, or at least measurably reduced, by heeding certain dictums of personal hygiene, by providing adequate nutrition and hemopoietic stimuli. Physicians should be more conscious of the possibility of strongyloidiasis; they should make their diagnosis as early as possible and carry out specific therapy until the infection is eradicated.

Treatment of Oxyuriasis.—D'Antoni and Sawitz studied the efficacy of gentian violet for oxyuriasis patients in an institutional environment. The investigations were made on indigent or orphan children in three institutions in New Orleans. They were apparently healthy white males and females from 3 to 21 years of age but mostly from 11 to 17 years. The diagnosis of oxyuriasis was based on the NIH swab (Hall's cellophane-tipped glass rod) technic. The persons examined were considered free from pinworms only after seven negative NIH swabs. The seven posttreatment swabs were taken within twenty-six days following treatment. In one home 38 per cent of the children (twenty-three girls and thirty-five boys) were found infested with Enterobius vermicularis. Rigid hygienic measures were carried out over a period of six weeks, but a 13 per cent increase in incidence occurred. In another home 97 per cent of 122 boys, and in the third home 81 per cent of twenty-six girls were found infested. Treatment of the infested boys and girls with coated half grain tablets of gentian violet medicinal in varying dosages resulted in a cure of approximately 90 per cent. The untoward symptoms of gentian violet medication were not serious. Vomiting occurred in a high percentage, but its frequency was low when computed on a basis of the total number of doses of the drug. It was found to occur more frequently in females than in males. The authors emphasize the difference between the cure of the individual with gentian violet and the eradication of an infestation in an institution.

American Review of Tuberculosis, New York

41:675-832 (June) 1940

*Results of Extrapleural Thoracoplasty for Pulmonary Tuberculosis. G. N. J. Sommer Jr., Trenton, N. J., and A. A. Ehler, Albany, N. Y.—p. 675.
Tuberculous Tracheobronchitis: A Review. R. S. Jenks, Mount Morris, N. Y.—p. 692.
Routine Bronchoscopy in Tuberculosis. J. C. Sharp and C. B. Gorham, Salinas, Calif.—p. 708.
*Cystic Lungs. S. Diamond, Legion, Texas, and W. R. Durham, Oteen, N. C.—p. 719.
Sulfapyridine in Experimental Tuberculosis: Pathology of Experimental Tuberculosis and of Apparent Toxic Changes in Guinea Pigs Treated with Sulfapyridine. W. H. Feldman and H. C. Hinshaw, Rochester, Minn.—p. 732.
Progressive Primary Tuberculous Complex. M. R. Louria, New York.—p. 751.
Anorectal Tuberculosis. G. H. C. Joynt, London, Ont.—p. 760.
Incidence of Tuberculosis Among Students at Lund University. E. Hedvall, Lund, Sweden.—p. 770.
Tuberculosis Survey of San Bernardino County. E. Bogen, Olive View, Calif.—p. 781.
Case Finding. W. H. Hatfield, Vancouver, B. C.—p. 784.
Medicolegal Aspects of Silicosis. T. C. Waters, Baltimore.—p. 792.

Extrapleural Thoracoplasty and Tuberculosis.—Sommer and Ehler determined the influence of certain conditions on the results of extrapleural thoracoplasty for pulmonary tuberculosis in 177 patients. Seven patients died from causes directly or indirectly connected with operation, one patient committed suicide and thirteen patients died after their discharge to sanatoriums or their homes; 140 patients have closed cavities and sputums negative for tubercle bacilli and fifteen living patients have positive sputum. Of the 176 traced patients 155 are

living, the average length of follow-up being thirty and one half months. Of these living patients 140 have closed cavities and negative sputums. No patient has been considered quiescent unless his sputum has been negative on examinations of concentrated specimens and cultures for at least six months. Twenty-eight patients are classified as apparently cured, fifty-five as arrested, forty as apparently arrested, fifteen as quiescent and two as improved. These two patients are classified as only improved in spite of closed cavities and negative sputums as one is dyspneic and the other is thought by her physician to have a blocked cavity. Ninety-four of the 140 patients with closed cavities and negative sputums are now working full time or part time or are able to work. Only the seventeen patients classified as quiescent or improved remain in sanatoriums. While the size of the pulmonary cavities appears to be of significance in affecting the results of thoracoplasty, more important factors are incomplete operation, contralateral active tuberculosis and early regeneration of resected ribs. The patient's age, duration of tuberculosis, the presence of pneumothorax with or without effusion or empyema and the position of the cavities in the lungs are of relatively little significance.

Cystic Lungs.—Diamond and Durham report ten cases of cystic disease of the lungs. Six of these were encountered within a period of nine months among approximately 1,500 consecutive general hospital admissions. Recent observations seem to indicate that truly congenital cysts are less frequent than was formerly thought. A careful history and frequently repeated examinations often suggest the pathogenesis of acquired cystic disease in individual patients. The structural variations among cystic lungs are as marked as are the differences in their etiology. Cysts may be single or multiple, unilocular or multilocular. They may be present in any part of one or both lungs. The condition occurs about as often in the two sexes. The cysts range in size from tiny sacs to incredibly huge air pockets. Roentgenographically, air cysts appear simply as areas of increased illumination in which normal lung markings are absent. When several are situated close to one another, their condensed septums may appear as very fine straight or curved lines, giving the appearance of a large honeycomb. It is often difficult to distinguish an air cyst from a pneumothorax. It may become necessary to induce a diagnostic pneumothorax to make a diagnosis. The authors have not been able to introduce iodized poppy-seed oil into these cysts through endobronchial catheters. The oil failed to flow beyond one of the larger bronchial radicles, suggesting that the bronchial opening of these cysts must be exceedingly small, in contrast to that present in typical bronchiectatic cavities. Cystic lungs have no distinctive clinical picture and may occur at any age. Many patients are symptom free throughout their lives, the lesion being discovered during a routine physical or x-ray examination. The clinical manifestations may be quite pronounced. The severity of the symptoms in uncomplicated cases apparently is determined by the extent of actual loss of pulmonary tissue and intracystic pressure. As the effective breathing space is encroached on, the patient becomes dyspneic; the greater the reduction of his vital capacity, the more uncomfortable he becomes. This dyspnea, caused by permanent absence of parenchymal tissue, is continuous. Complications, infection of the cyst or its rupture into the pleural space, are relatively rare; when they do occur the clinical picture of the secondary process usually supersedes that occasioned by the cystic disease. The ten patients discussed saw arduous military service during the World War. At the time of their enlistment these men were presumably free of symptoms. Four of the patients had but one cyst and six had more than one. The condition was found in the left lung in two, in the right in two and in both lungs in six patients. The upper and lower thirds of the lungs were involved with approximately equal frequency, the middle thirds less often. Six men gave a history of previous respiratory disease. The four patients with no symptoms attributable to their cystic disease had only a small, solitary cyst. Two patients suffered for years from a persistent, unvarying dyspnea and numerous cysts were present in both. The four remaining patients gave a history of gradually increasing dyspnea. Two of these died; postmortem examination of one demonstrated that cystic disease was the cause of death.

Archives of Dermatology and Syphilology, Chicago

41:1001-1224 (June) 1940

*Dermatomyositis: Study of Forty Cases. P. A. O'Leary and M. Waisman, Rochester, Minn.—p. 1001.
Eczema of Ear Associated with a Diphtheria-like Organism: Report of Case. J. J. Eller and L. H. Kest, New York.—p. 1020.
Superficial Noninflammatory Lesions of the Feet: Demonstration in Sections of a Fungus of the Genus Actinomyces. H. Sutherland-Campbell, Los Angeles.—p. 1023.
Whealing Capacity of Skin of Newborn or Young Infant: Report of Experiments. M. B. Sulzberger and R. L. Baer, New York.—p. 1029.
Erysipeloid: Report of Case. R. B. Grinnan and W. B. Martin, Norfolk, Va.—p. 1037.
Eruptions and Photosensitivity Due to Dyed Fabrics. E. Epstein, Oakland, Calif.—p. 1044.
Acute Arthritis Associated with Myocarditis Simulating Acute Lupus Erythematosus: Report of Case. H. C. Gotshalk and J. T. Wayson, Honolulu, Territory of Hawaii.—p. 1053.
Clavicle Sign of Late Congenital Syphilis: Review of Literature and Report of Six Cases. K. L. Yang, Shanghai, China.—p. 1060.
Erythema Exsudativum Multiforme (Hebra) with Conjunctivitis and Stomatitis. L. Rosenberg and J. Rosenberg, Brooklyn.—p. 1066.
Cases of Familial and of Conjugal Pemphigus Vulgaris: Use of Transfusions of Blood from Cured Patients. S. S. Greenbaum, Philadelphia.—p. 1073.
Erythema of Ninth Day Following Bismuth Therapy for Syphilis. J. L. Grund, Boston.—p. 1076.
Acute Syphilitic Transverse Myelitis: Clinical Study and Report of Case. S. Berman, Northport, N. Y.—p. 1078.
The Sudoriparous Glands: III. Sweat. S. C. Way, San Francisco, and A. Memmesheimer, Essen, Germany.—p. 1086.

Dermatomyositis.—According to O'Leary and Waisman, between 1926 and 1939 forty unquestionable cases of subacute and chronic dermatomyositis were observed at the Mayo Clinic. A history of acute infection (tonsillitis, influenza and sinusitis) antedated the onset of the dermatomyositis in eleven. Recent parturition preceded the disease in three. Chronic diseases, including pulmonary tuberculosis, bronchiectasis, rheumatic fever, recurrent furunculosis and infectious arthritis, were observed in ten others. Adenocarcinoma of the rectum with metastasis to the liver was associated in one case. Dermatomyositis may be heralded by muscular, cutaneous or vasomotor signs. The most common early complaint among eighteen patients was muscular pain and weakness, and in fourteen edema and cutaneous lesions ushered in the disease. In six other cases muscular and dermatologic symptoms were initially combined in the form of eruption (or edema) and weakness, with or without pain. Vasomotor phenomena were observed in two cases before symptoms referable to the skin or to the musculature appeared. The muscular involvement was not regular or constant in sequence. Usually the myositis was characterized by a nearly symmetrical bilateral involvement. The consistency of the muscles may be normal, soft and doughy or tough, firm and fibrous. Muscular atrophy usually developed in cases of longer duration, and dermatomyositis was frequently associated with muscular contractures and "fixed joints." The deep reflexes were occasionally normal, but more often they were decreased or absent. The vital striated musculature (pharynx, larynx, intercostal muscles and diaphragm) was involved and this was an extremely serious complication. Twenty-seven patients experienced dysphagia. Thirteen exhibited vocal changes; hoarseness or altered pitch. Ten patients experienced frank dyspnea. Weakness and tremor of the tongue occurred in six and diplopia was complained of by four. Occasionally cutaneous changes are absent, but in most cases they are prominent and include erythema, edema, pigmentation, sclerosis, atrophy, lupus erythematosus-like efflorescence and poikiloderma atrophicans vasculare. The systemic reaction is indicated in some cases by fever. Approximately half the patients have died. The sexes were nearly equally represented. No age was exempt, but there were more patients in the fifth decade. The onset was more common (sixteen) in the summer. Various micro-organisms have been incriminated, generally streptococci and staphylococci. Dermatomyositis may be caused by various bacterial factors either as a direct invasion by way of the blood stream or as a toxic effect of bacterial products on the reacting tissues. Microscopic study of the earliest lesions of muscles indicates that the primary reaction may be manifested by the sarcoplasm rather than by interstitial cellular infiltration. As a rule the tempo of the onset signifies the rapidity of the course that will follow. Of thirty-eight patients followed, nineteen died in from four months to six years. Four patients have recovered completely. The dermatomyositis of none of these

was severe. In seven cases the condition has improved or is stationary, although accompanied by a variable amount of muscular incapacity. Of the eight patients whose condition has not improved, two have been observed too recently to permit comment on the course of the disease, three have suffered relapses and three have reported a slow, steady increase of weakness. Diagnostic problems are provided mostly by the early forms of the disease before distinctive muscular and cutaneous signs develop. Most difficult to distinguish from dermatomyositis are diffuse scleroderma in its edematous stage and scleredema adultorum (Buschke). Other disorders to be differentiated are trichinosis, pellagra and lupus erythematosus. The course of dermatomyositis may at times simulate polyneuritis, myasthenia gravis, the myopathies, panniculitis, purulent embolic (septic) myositis, erysipelas, Addison's disease, acute rheumatic fever, periarteritis nodosa, postinfectious asthenias and functional states of exhaustion. Treatment of this disease of unknown cause is solely empirical and symptomatic. It includes the administration of vaccines, aminoacetic acid and sulfanilamide. At present a combination of artificial fever therapy, inhalations of oxygen and physical therapy appear most promising.

Archives of Neurology and Psychiatry, Chicago

43:1057-1298 (June) 1940

*"Bulgarian Treatment" of Parkinson's Disease: Pharmacologic Aspects and Clinical Effects of Alkaloids of Belladonna Root. H. Vollmer, New York.—p. 1057.

Personality Changes Accompanying Cerebral Lesions: II. Rorschach Studies of Patients with Focal Epilepsy. M. R. Harrower-Erickson, Montreal.—p. 1081.

Neurohistopathologic Changes with Metrazol and Insulin Shock Therapy: Experimental Study on Cat. N. W. Winkelman and M. T. Moore, Philadelphia.—p. 1108.

Histologic Variations with Age in Apparently Normal Peripheral Nerve Trunks. Lillian Cottrell, Minneapolis.—p. 1138.

Cerebral Air Embolism and Vital Staining: Contribution to Experimental Study of Blood-Brain Barrier. S. M. Bouton Jr., Wrentham, Mass.—p. 1151.

Convulsions Associated with Tumors of Cerebellum: Clinical and Pathophysiologic Features. J. E. Webster and L. M. Weinberger, Philadelphia.—p. 1163.

Visuopsychic Apparatus and Accommodation Reflex. R. Y. Herren, Portland, Ore.—p. 1185.

Apparent Dedifferentiation of Nerve Cells of Human Brain as Result of Prolonged Starvation. W. Andrew, Dallas, Texas.—p. 1188.

Craniopharyngioma in Third Ventricle of Brain: Partial Surgical Removal and Pathologic Study. H. Zeitlin and E. Oldberg, Chicago.—p. 1195.

Sealing Specimens of Brain with Pliofilm: Practical and Inexpensive Way to Exhibit Specimens. L. W. Darrah, Northampton, Mass.—p. 1205.

Direct Psychotherapy of Children. M. Gitelson, Chicago.—p. 1208.

"Bulgarian Treatment" of Parkinsonism.—Vollmer tried the principal three alkaloids of belladonna root, hyoscyamine, scopolamine and atropine, in a synthetic compound in systematically varied and different combinations in the treatment of thirty patients with Parkinson's disease. The studies indicated that the range of greatest efficacy with the smallest possible dose was a combination of the three alkaloids in the following proportions: hyoscyamine from 75 to 95 per cent, atropine from 5 to 15 per cent and scopolamine from 1 to 5 per cent. An empirical combination consisting of hyoscyamine hydrobromide 90.2 per cent, atropine sulfate 7.4 per cent and scopolamine hydrobromide 2.4 per cent seemed particularly effective and was preferred by 90 per cent of the patients. This alkaloid compound was made up as an aqueous-alcoholic solution containing 3 mg. of total alkaloids per cubic centimeter and 66 per cent alcohol. Tablets of identical composition were also prepared, each containing 0.5 mg. of total alkaloids. One of these tablets corresponded quantitatively to four or five drops of the aqueous-alcoholic solution. This synthetic compound proved to be of at least the same efficacy as the most effective natural extracts of Bulgarian roots. On the basis of this definite clinical observation any obscure suppositions or mystic implications (nature healing) about the Bulgarian treatment can be dismissed. An average daily dose of from 2 to 3 mg. of this alkaloid compound was necessary to obtain an optimal clinical result. A pharmacodynamic synergism of the three alkaloids must be assumed. Even with this assumption, the effect on the central nervous system in parkinsonism cannot be explained. Nevertheless a combination of these alkaloids brings about striking results. The treatment should be started with very small doses, which are gradually increased. All other medication must be discontinued. The required dose for each patient varies from one half to seven tablets three times a day but ranges on the average from one and one half to two tablets three times a day, or from 2.25 to 3 mg. of total alkaloids daily. Slight dizziness, dryness of the throat or sluggishness are occasionally described by the patients and are signs of overdosage. Not all symptoms of the disease respond to the drug simultaneously or to the same extent. General spirits and muscular rigidity are the first to respond. Parkinsonian patients are sensitive, good natured, trustful, thankful and cooperative and have a strong desire to get well. It is important to encourage them until obvious clinical improvement is obtained. Hopelessness and skepticism delay the objective improvement. Fifty-two patients were treated, thirty-four of whom had postencephalitic parkinsonism and eighteen nonencephalitic paralysis agitans. Fifty per cent of the postencephalitic but only 17 per cent of the nonencephalitic patients were markedly improved. There was moderate improvement in a further 32 and 33 per cent of the two respective groups. Four patients who had chronic encephalitis became entirely free from symptoms. In nonencephalitic parkinsonism only partial relief can be expected. Nevertheless, even this limited improvement may turn a complete invalid into a person who can enjoy some degree of independence and take part in some activities. The majority of the improved patients were able to work. Treatment with the belladonna alkaloid compound is symptomatic and must be continued indefinitely. Supplementary psychotherapy is valuable.

Delaware State Medical Journal, Wilmington

12:73-136 (May) 1940

Crime and Psychiatry. M. A. Tarumianz, Farnhurst.—p. 73.

Endocrine Therapy in Mongolian Idiocy. C. W. Dunn, Philadelphia.—p. 78.

Need for More Physical Study of Mental Cases. P. F. Elfeld, Farnhurst.—p. 84.

Adrenal Neurocytoma. J. W. Ballard, Farnhurst.—p. 86.

Psychosis Following Secondary Anemia: Report of Two Cases. F. Paul, Farnhurst.—p. 89.

The General Practitioner and Psychiatry. H. W. Mikkelsen, Farnhurst.—p. 91.

Functional Psychosis and Brain Tumor. G. J. Gordon, Farnhurst.—p. 93.

Insufficiency in Adrenal Cortex. F. Freytag, Farnhurst.—p. 96.

Psychosis Associated with Psychopathic Constitution. M. Zimbler, Farnhurst.—p. 99.

Preventive Psychiatry: Presentation of Two Cases from the Child Guidance Clinic to Illustrate Treatment Methods. M. L. Wadsworth, Farnhurst.—p. 103.

Surgical Aspects of Essential Hypertension. G. Bieringer, Farnhurst.—p. 108.

Importance of the Art Department for the Interpretation of Psychic States. F. Freyhan, Farnhurst.—p. 111.

Sulfanilamide—Local Application in Dentistry. W. H. Norris, J. A. Wiener and I. L Yalisove.—p. 118.

Journal of Pharmacology & Exper. Therap., Baltimore

69:1-102 (May) 1940. **Partial Index**

Studies of Actions of Methyl-Adrenalin; Methadren. J. W. Stutzman and O. S. Orth, Madison, Wis.—p. 1.

Toxicologic Studies on Cubé. H. B. Haag and Isabel Taliaferro, Richmond, Va.—p. 13.

Influence of Hydrogen Ion Concentration on Absorption of Alkaloids from Stomach. Janet Travell, New York.—p. 21.

Acetylation of Sulfanilamide and Sulfapyridine in Cat. W. Van Winkle Jr. and W. C. Cutting, San Francisco.—p. 40.

Comparison of Coronary Vasodilator Activity of Certain Alkyl Xanthines. G. V. LeRoy and J. H. Speer, Chicago.—p. 45.

Respiratory Alkalosis During Anesthesia: III. Hemoglobinemia Following Prolonged Hyperventilation. R. T. Stormont, M. H. Seevers, F. E. Shideman and T. J. Becker, Madison, Wis.—p. 68.

Therapeutics of Experimental Hypertension. A. Grollman, Baltimore; T. R. Harrison and J. R. Williams Jr., Nashville, Tenn.—p. 76.

Clinical Comparison of Picrotoxin, Metrazol and Coriamyrtin Used as Analeptics and as Convulsants. W. J. Bleckwenn, E. R. Hodgson and R. P. Herwick, Madison, Wis.—p. 81.

Comparative Therapeutic Activity of Sulfanilamide, Sulfapyridine and Diaminosulfone in Streptococcus Infections in Mice. E. K. Marshall Jr., J. T. Litchfield Jr. and H. J. White, Baltimore.—p. 89.

Journal of Urology, Baltimore

43:767-930 (June) 1940. Partial Index

Hypernephroma in Polycystic Kidney: Review of Literature and Report of Case. M. M. Melicow and H. H. Gile, New York.—p. 767.
*Staphylococcic Infections of Renal Cortex: Analysis of Five Additional Cases of Carbuncle and Six Additional Cases of Abscess. P. J. Kahle, M. M. Green and G. Tomskey, New Orleans.—p. 774.
Some Aspects of Pathology of Pyelonephritis. W. G. J. Putschar, Charleston, W. Va.—p. 793.
Lymph Collectors from Ureters, Their Regional Nodes and Relations to Posterior Abdominal Lymph Channels. Alice E. Parker, Denver.—p. 811.
Urethrography in Bulbo-Urethral Adenitis. M. L. Brodny and S. A. Robins, Boston.—p. 844.
*Tumors of Testis: Study of Pathology of 142 Cases of Primary Neoplasms of Testis in Man. W. G. Gordon, Ann Arbor, Mich.—p. 851.
Initial Priapism During Therapy with Testosterone Propionate in Eunuchoid Man. Rita S. Finkler, Newark, N. J.—p. 866.
Male Infertility from Gynecologic Point of View. S. R. Meaker, Boston.—p. 871.
Histaminase and Histamine Desensitization in Genito-Urinary Allergy. H. M. Johnson, San Antonio, Texas.—p. 891.
Study of Bactericidal Activity of Sulfanilamide in Urine at Various Levels of Hydrogen Ion Concentration. J. R. Sickler, Rochester, Minn.—p. 906.

Staphylococcic Infections of Renal Cortex.—Kahle and his colleagues add five cases of renal carbuncle to the two reported in 1933 and also report six cases of renal cortical abscess. These eleven cases were encountered at Charity Hospital during a period of three years. In the authors' opinion the lesions of the renal cortex are not identical with renal carbuncle and do not, as some authors claim, represent separate stages of the same lesion. They may be single or multiple. Pathologically they differ in many respects. The distinction was particularly well marked in one case in which there was a carbuncle of the upper pole of the kidney and multiple discrete abscesses elsewhere in the renal cortex. The abscesses were widely separated from the carbuncle and from one another and presented none of the characteristics of the carbuncle. Both lesions are undoubtedly the result of blood borne infection, but the carbuncle, because of its wedge shape, probably arises from occlusion of an artery by septic embolus; later the infarction goes on to suppuration. The abscess is probably caused by bacteria which have lodged in a glomerulus without complete occlusion. Later central necrosis and abscess formation occur at this point. The origin of the renal infection is a primary focus. A history of a previous carbuncle, furuncle, paronychia, tonsillar infection, trauma or infection of a simple cut was elicited in eight of the eleven cases. From eight to twelve weeks elapsed before symptoms of cortical renal infection ensued. The carbuncle is separated from the cortex by a wall of thick fibrous tissue. The suppurating areas, which vary in size, may or may not connect with one another and the craters never contain large amounts of pus. The lesion is not fluctuant and is hard to the touch. The suppurating craters contain thick creamy or greenish pus. The base is somewhat raised above the surface of the kidney, and the overlying capsular tissue is thick and greatly infiltrated. The cortical abscess is round or oval. Fluctuation can be made out even when it is tense, and the characteristic induration of the carbuncle is lacking. When the lesion is close to the surface of the kidney, areas of dirty white or creamy hyperemia surround it. When the lesion ruptures or is incised and purulent contents are completely evacuated, the cavity is rather soft and smooth to the touch. Staphylococcus aureus was found in seven cases and Staphylococcus albus in three of the ten in which such study was made. Treatment is essentially surgical, but radical operation is not always necessary. A lower mortality usually follows nephrectomy, but excellent results can be achieved by conservative procedures in properly selected cases. Early diagnosis and prompt surgical intervention decrease the mortality and the postoperative morbidity. The time element is therefore an important factor in the final outcome.

Tumors of Testis.—Gordon analyzed the pathologic material of 142 primary neoplasms of the testis in an endeavor to interpret their pathogenesis. Special attention was given to the histopathology of the tumors and the presence of teratomatous structures. Any tumor was considered to be of teratomatous origin if tissues were demonstrated in it which could not conceivably have arisen from adult germinal epithelium or normal testicular supporting tissues by anaplastic or metaplastic changes. Therefore such structures as striated muscle, cartilage, mucin-forming columnar epithelium or any malignant neoplasm derived from these, as a mucin-forming adenocarcinoma, were considered to be teratomatous in origin. Eighty of the 142 tumors were of teratomatous origin and in sixty-two this origin was not proved. The author states that the evidence favors the hypothesis that essentially all neoplasms of the testis are of teratomatous origin, with cellular overgrowth of one germ layer often producing homogeneous neoplasms which resemble germinal epithelium. Careful search will reveal teratomatous remains in many characteristic neoplasms of this type, which cannot be distinguished microscopically from those in which teratomatous elements cannot be found. The occurrence of teratomatous elements exceeds the expected incidence of coexistence of two primary neoplasms in the same organ, and therefore the teratoma should be accepted as significant of the pathogenesis. No transition stages were found between normal germinal epithelium and embryonal carcinoma (seminoma) or adenocarcinoma. The study offers no additional evidence as to the origin of teratomas in the testis.

Kansas Medical Society Journal, Topeka

41:189-232 (May) 1940

Rose Operation: Repair of Trigonal Muscle (Incontinence in the Female). F. W. Matassarin, Wichita.—p. 189.
Artificial Fever Therapy. L. F. Glaser, Kansas City.—p. 192.
Clinical Illustration of Acid-Base Imbalance. F. C. Neff, Kansas City, Mo.—p. 196.
Ten Year Statistical Study of Cesarean Section in Sedgwick County. R. H. Maxwell, Wichita.—p. 199.

Laryngoscope, St. Louis

50:373-502 (May) 1940

Progressive Deafness, Otosclerosis and Closely Related Subjects: Abstract of Available Literature Published During the Year 1939. J. A. Babbitt, Philadelphia.—p. 385.
Stenosis of Larynx Due to Paralysis of Vocal Cords: Treatment by Submucous Resection of Vocal Cords: Report of Operated Cases. J. H. Maxwell, Ann Arbor, Mich.—p. 452.
Pathologic Conditions of Esophagus. L. H. Clerf, Philadelphia.—p. 463.
Hoarseness: New Classification and Brief Report of Four Interesting Cases. D. I. Frank, New York.—p. 472.
Otorhinologic Sequelae of Swimming: Analysis of Present Concepts: New Method of Prevention. D. Mezz, Brooklyn.—p. 479.

Medicine, Baltimore

19:161-328 (May) 1940

Uric Acid Content in Blood and Urine in Health and Disease. K. Brøchner-Mortensen, Copenhagen, Denmark.—p. 161.
Acute Hemolytic Anemia (Acquired Hemolytic Icterus, Acute Type). W. Dameshek and S. O. Schwartz, Boston.—p. 231.

New England Journal of Medicine, Boston

222:901-942 (May 30) 1940

Immunity to Virus Diseases: Some Theoretical and Practical Considerations. E. W. Goodpasture, Nashville, Tenn.—p. 901.
Hydronephrosis: Standardization of Surgical Treatment. T. E. Gibson, San Francisco.—p. 910.
Appendices Epiploicae. G. A. Moore, Brockton, Mass.—p. 919.

222:943-984 (June 6) 1940

Blood Phosphorus Studies in Rheumatic Fever. N. Epstein and F. C. McDonald, Boston.—p. 943.
End Results of Use of Large Doses of Amphetamine Sulfate over Prolonged Periods. W. Bloomberg, Boston.—p. 946.
*Prevention and Management of Pain Following Cholecystectomy. J. M. McGowan and F. F. Henderson, Boston.—p. 948.
Importance of Investigating Cause of Renal Pain. H. G. Nichols, Haverhill, Mass.—p. 954.

Pain Following Cholecystectomy.—McGowan and Henderson point out that, after surgical removal of the gallbladder, pain and discomfort often return and are as severe as they were before the operation. Biliary colic following cholecystectomy is due to obstruction of the common duct, preventing the flow of bile into the duodenum. Obstruction of the common duct may be due to stone, stricture, edema or spasm. The back pressure results in pain. Common duct pressure of 70 mm. of water produces pain in some individuals, while 500 mm. may be withstood by others with impunity. Prolonged T-tube drainage allows the common duct to resist greater pressures. Glyceryl trinitrate relaxes duodenal spasm and tends to lower

the intrabiliary pressure. The authors describe methods for studying the patency of the papilla of Vater and the condition of the bile ducts. They show that biliary dyskinesia and many symptoms of cholecystitis are relieved by a course of treatment consisting of the daily use of glyceryl trinitrate to relax duodenal spasm.

New Orleans Medical and Surgical Journal

92:665-730 (June) 1940

Angina Pectoris and Coronary Thrombosis. W. R. Wirth, New Orleans.—p. 671.
Plasma Proteins: Methods of Determination and Clinical Significance. H. H. Beard, New Orleans.—p. 678.
Effects of War on Mental Health. C. S. Holbrook, New Orleans.—p. 681.
Acute Epidural Abscess of Spinal Canal. D. H. Echols, New Orleans.—p. 682.
Acute Spontaneous Cerebral Vascular Accidents in Adults: Review. L. K. Levy, New Orleans.—p. 683.
Vincent's Cervicitis. J. P. Quindlen and L. Taubenhaus, Brooklyn.—p. 692.
Treatment of Tularemia with Thiazole Derivatives of Sulfanilamide. J. O. Weilbaecher Jr. and Emma S. Moss, New Orleans.—p. 694.
Modern Medical Illustrating. T. Jones, Chicago.—p. 697.
Francesco Antommarchi (1780-1838). R. Glenk, New Orleans.—p. 701.

New York State Journal of Medicine, New York

40:837-908 (June 1) 1940

*Ambulatory Insulin Treatment of Mental Disorders. P. Polatin, H. Spotnitz and B. Wiesel, New York.—p. 843.
Acute Putrid Abscess of Lung—Surgical Disease. H. Neuhof and A. S. W. Touroff, New York.—p. 849.
Use of Tubed Pedicle Flaps for Study of Wound Healing in Human Skin. L. E. Sutton, Syracuse.—p. 852.
Pulmonary Apical Tumefaction Simulating Bursitis: Necessity for Routine Chest Examination in Patients with Shoulder Pain. L. Nathanson, Brooklyn.—p. 860.
Modern Concepts of Mental Illnesses. G. S. Sprague, White Plains.—p. 865.
Infected Renal Cyst. B. Davidson, Brooklyn.—p. 875.
Rapid Method for Checking Position of Tube During Gastric Gavage. E. Messinger, Brooklyn.—p. 882.
A New Skin Thermometer. S. S. Samuels, New York.—p. 884.
Let Us Wassermannize the Expectant Father. M. Berlind, Brooklyn.—p. 885.

Ambulatory Insulin Treatment of Mental Disorders.—Polatin and his associates gave small doses of insulin hypodermically to twenty-two unselected patients with mental disease of functional or organic type. The functional group included eighteen patients with schizophrenia, manic-depressive psychosis or psychoneurosis. The organic group consisted of four patients with definite cerebral lesions associated with hypertensive cardiovascular disease, cerebral arteriosclerosis, an organic syndrome following removal of a pineal tumor or organic brain disease of an undetermined type. Patients were given one hypodermic injection of insulin daily at 5 a. m. and had the usual hospital breakfast at 8 o'clock. The initial dose was 5 units. This was increased daily by 5 units until a mild hypoglycemic shock, characterized by usual symptoms of weakness, giddiness, tachycardia, vasomotor alterations, excessive perspiration and some drowsiness, was obtained. Usually the hypoglycemic symptoms began about two hours after the injection and gradually increased in severity. Hypoglycemia was permitted for from fifteen to forty-five minutes. The 40 units of insulin in one dose was sufficient to produce the desired effect. The hypoglycemic state was usually terminated with breakfast. During hypoglycemia the patients were up and about. The mild hypoglycemic symptoms did not prevent the patients from feeding themselves at breakfast without any assistance. The twenty-two patients were treated over a period ranging from one week to eighteen months. Transitory alterations in the mental status of the patients were observed during the daily treatment period and in some instances continued for a few hours thereafter. Agitated and excited patients were quieted, states of confusion were cleared, and dulness and apathy gave way to increased alertness. Such beneficial changes gradually persisted for longer periods after each treatment until definite clinical improvement was maintained. Even the four unimproved patients were influenced sufficiently by the insulin treatment so that nursing and feeding problems were simplified. All patients gained weight with an accompanying increase in appetite. One patient recovered, twelve were much improved and five were slightly improved. The much improved patients were able, despite residual symptoms, to adjust themselves socially at a level paralleling their premorbid behavior. The slightly improved patients showed a definitely increased ability to adjust themselves to the hospital routine but did not reach their premorbid behavior level because of residual symptoms. No coma, allergic manifestations, convulsions or observable injuries occurred during treatment.

Northwest Medicine, Seattle

39:199-234 (June) 1940

Hypertension. N. C. Gilbert, Chicago.—p. 202.
Allergic Skin Disorders: Practical Approach to Their Management. F. Perlman, Portland, Ore.—p. 205.
Vitamin Therapy in Dermatologic Practice. T. S. Saunders, Portland, Ore.—p. 209.
Treatment of Certain Allergic Skin Conditions with Histaminase. A. R. Altose, Seattle.—p. 212.
Histaminase in Treatment of Peptic Ulcer. P. O'Hollaren, Seattle.—p. 216.
Calcification of Pericardium: Edema of Head and Neck a Symptom. C. I. Drummond, Medford, Ore.—p. 217.
Bilateral Anterior Lenticonus, with Congenital Discoid Punctate Cataracts. C. F. Harris, Klamath Falls, Ore.—p. 219.
Ideal Vaccination Technic. H. M. Page, Portland, Ore.—p. 220.
Pneumococcic Meningitis Treated Successfully: Case Report. S. Vukov, Seattle.—p. 221.

Ohio State Medical Journal, Columbus

36:585-712 (June) 1940

Anxiety Neurosis. H. Evans and G. T. Harding, Columbus.—p. 601.
Cancer of Body of Uterus. T. H. George, Cleveland.—p. 606.
Exercise in Tuberculosis: Plea for Conservatism. W. J. Habeeb, Mount Vernon.—p. 609.
Volvulus: Case Report. J. J. Marek, Cleveland.—p. 611.
Early Diagnosis of Syphilitic Aortitis. J. W. Martin, Cleveland.—p. 612.
Cleveland City Hospital Observations on Sources of Infection in Syphilis. H. E. Freeman, Cleveland.—p. 616.
Compression of Upper Ureter by Metastatic Embryonal Carcinoma of Periureteral Lymph Node, Primary in Testis. W. Rosenberg, Cleveland.—p. 620.
Selection and Management of Anesthesia for Upper Abdominal Surgery. J. D. Spaid, Dayton.—p. 624.
Treatment of Cancer of Nose and Throat. E. King, Cincinnati.—p. 627.
Mucocele of Appendix. C. B. Elliott, Painesville.—p. 629.
Rheumatic Fever in Children. R. A. Lyon, Cincinnati.—p. 631.
Chronic Acetanilid Poisoning: Report of Case. N. Michael, Columbus.—p. 632.

Pennsylvania Medical Journal, Harrisburg

43:1249-1376 (June) 1940

The Neurogenic Bladder. R. M. Nesbit and W. G. Gordon, Ann Arbor, Mich.—p. 1261.
Psychotic Manifestations in Physical Disease and in Reaction to Drug Therapy. A. P. Noyes, Norristown.—p. 1269.
Safety Measures in Intracapsular Cataract Extraction. H. E. Thorpe, Pittsburgh.—p. 1280.
Antisepticized Hose as an Aid in Pedal Acromycosis. S. S. Greenbaum and J. W. E. Harrisson, Philadelphia.—p. 1289.
Amaurotic Family Idiocy. G. J. Feldstein, Pittsburgh.—p. 1296.
Prescribing a Hearing Aid. K. M. Day, Pittsburgh.—p. 1299.
Empyema in Children. E. W. Meredith, Pittsburgh.—p. 1303.
*Treatment of Empyema with Hydroxyethylapocupreine Dihydrochloride. Maud L. Menten and R. R. MacDonald, Pittsburgh.—p. 1305.

Hydroxyethylapocupreine Dihydrochloride for Empyema.—Menten and MacDonald treated twenty-five children suffering from empyema with hydroxyethylapocupreine dihydrochloride. From 25 to 150 cc. of the drug, preferably dissolved in a slightly alkaline solution in a concentration of 1 per cent, was injected and left in the empyema cavity after a fairly complete evacuation of the pus was complemented by irrigation with the dissolved drug. Irrigation and instillation were repeated every third day. Usually after the second or third treatment the pus became sterile, the temperature returned to normal and the appetite improved. As the amount of pus progressively diminished, the temperature gradually approached normal. With evacuation and irrigation alone there was a temporary fall in temperature followed by prompt refilling of the empyema cavity with pus, which always gave a positive culture for pneumococcus. If the condition had existed for three or four weeks it usually did not respond to treatment as readily as when the disease was of shorter duration. The number of taps, combined with instillation of the drug, varied from three to twelve and the amount of drug used ranged from 195 to 1,200 cc. The

time required for cure varied from eleven to thirty-seven days, with an average of twenty-six days. Of the twenty-five children who received the closed treatment, nineteen were adequately and six were only partially treated. These six children were subsequently transferred to the surgical service for rib section. Fourteen of the nineteen patients responded favorably to treatment and were discharged completely cured. Three of the remaining five patients who failed to show favorable results had complicating pathologic disorders: an additional streptococcic infection, a recurrent pneumonia and an obscure abdominal condition. The drug therapy was ineffectual for the other two. The fourteen operated on (eight previously treated with the drug, two of the ineffectually and the six partially treated patients) were discharged from the hospital on an average of twenty-seven days after operation, returning to the dispensary for dressings. The average time required for the eradication of the empyema was approximately the same for the two. Hydroxyethylapocupreine dihydrochloride could undoubtedly be made more effective by the use of oxygen instillation to control pressures during evacuation of pus and by treating patients before the fibrin layers become too thick. More concentrated solutions of the drug for instillation and better technical removal of pus, as with Miller or Robinson pneumothorax needles, might shorten the time of treatment. Blood transfusions might be helpful in building up the child's resistance. The use of the drug is limited to pneumococcic empyemas and to cases in which no inaccessible encysted pus is present.

Public Health Reports, Washington, D. C.

55:915-954 (May 24) 1940

Determination of V Factor in Urine and Tissues of Normal Dogs and of Dogs with Blacktongue by Use of Haemophilus Parainfluenzae. Margaret Pittman and H. F. Fraser.—p. 915.
Two New Species of Argasidae (Acarina: Ixodoidea). R. A. Cooley and G. M. Kohls.—p. 925.

55:955-1002 (May 31) 1940

Prevalence of Poliomyelitis in the United States in 1939. C. C. Dauer.—p. 955.
The Course of Disabling Morbidity Among Industrial Workers, 1921-1938. W. M. Gafafer.—p. 962.
Studies of Sewage Purification: XIII. Biology of Sphaerotilus Natans Kutzing in Relation to Bulking of Activated Sludge. J. B. Lackey and Elsie Wattie.—p. 975.

Review of Gastroenterology, New York

7:203-304 (May-June) 1940

Splanchnoptosis as Potential Anatomic Path to Gastric and Duodenal Ulcer. Agnes C. Vietor, Boston.—p. 203.
Visceroptosis. M. G. Spiesman, Chicago.—p. 218.
Comparative Study of Methods Utilized to Determine Presence of Ulceration in Gastrointestinal Tract, with Special Note on the Woldman Phenolphthalein Test. A. L. Levin and M. Shushan, New Orleans.—p. 235.
Why Does Gastro-Enterostomy Fail? V. G. Burden, Philadelphia.—p. 242.
Tuberculosis of Retroperitoneal Lymph Nodes with Long Clinical Course of Obscure Fever. H. L. Rakov and J. S. Taylor, Kingston, N. Y.—p. 246.
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Rocky Mountain Medical Journal, Denver

37:393-472 (June) 1940

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Southern Surgeon, Atlanta, Ga.

9:381-458 (June) 1940

Cystoscopic Photography: Preliminary Report. E. G. Ballenger, H. P. McDonald and R. C. Coleman Jr., Atlanta, Ga.—p. 381.
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Surgery, Gynecology and Obstetrics, Chicago

70:987-1124 (June) 1940

*Effect of Zinc Peroxide Treatment on Ulcers Due to Micro-Aerophilic Hemolytic Streptococcus. T. A. Shallow, K. E. Fry and E. J. Pulaski, Philadelphia.—p. 987.
Clinical Use of Gonadotropic Hormone from Pregnant Mare Serum. C. P. Huber and M. E. Davis, Chicago.—p. 996.
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*Lung Abscess: Analysis of the Massachusetts General Hospital Cases from 1933 Through 1937. R. H. Sweet, Boston.—p. 1011.
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Preserved and Fresh Homotransplants of Cartilage. J. B. Brown, St. Louis.—p. 1079.
Carcinoma of Body of Uterus: Experience of the Mayo Clinic for Twenty-Four Years. J. C. Masson and R. O. Gregg, Rochester, Minn.—p. 1083.
Technic of Combined Division, Ligation and Injection of Incompetent Great Saphenous Vein. L. K. Stalker and W. W. Heyerdale, Rochester, Minn.—p. 1094.
Simple Nonspecific Ulcer of Jejuno-Ileum. D. R. Robinson and W. D. Wise, Baltimore.—p. 1097.
Ovarian Lesions Simulating Appendicitis. C. C. Guy and A. J. Rotondi, Chicago.—p. 1100.

Zinc Peroxide Treatment for Streptococcic Ulcers.—Shallow and his colleagues report six cases of chronic undermining ulcers due to the micro-aerophilic hemolytic streptococcus, stress the importance of early diagnosis, urge that anaerobic as well as aerobic cultures be requested as a routine in all cases with frank suppuration which fail to respond to ordinary measures and reaffirm the favorable influence of zinc peroxide cream dressings on the course of the infection. These infections went along for indefinite periods (up to two and one half years) unrecognized as to etiology. The physicians who first saw the patients believed that they were dealing with ordinary slow healing wounds. The patients were hospitalized only after trial and failure of the customary methods of treatment. The diagnoses were in many cases revised with lack of success with one treatment and substitution of another. Possibly because of the infrequent report of such cases in the literature, chronic undermining, burrowing ulcer was not mentioned early as a possible diagnosis. The fact that these ulcers may improve temporarily under various treatments is misleading and may tend to delay the true diagnosis. Their diagnosis is difficult unless anaerobic as well as aerobic bacteriologic studies are carried out. The invasive organism grows much better anaerobically than aerobically, at least early in the disease. It may be missed on the aerobic plates, especially in the presence of rapidly growing secondary contaminants. The same holds true in long standing infections in which the colonies of hemolytic streptococci growing on the aerobic plates are few in number. Therefore material from the ulcers should be planted immediately on mediums under anaerobic as well as aerobic conditions. It is practicable to advise the laboratory to search for the micro-

aerophilic hemolytic streptococcus. One of the authors' cases is representative of the way these infections may continue for months or years with extensive destruction of tissues before the true cause is recognized. The disease began as a trivial abrasion and spread with involvement of the surrounding skin and subcutaneous tissues until there was extensive destruction. The failure to heal was attributed to the presence of syphilis. When syphilitic therapy in conjunction with various antiseptics failed to effect a cure, a diagnosis of stasis ulcer was made. The regressions were explained on the basis of secondary infection. Each time that the acute infection subsided the patient was discharged (six times) from the hospital and was treated as an ambulatory case. It was not until the fifth admission that further possibilities were looked into, and this after two amputations and several débridements had already been made. An earlier diagnosis might have been made had there been (1) true appreciation of the clinical manifestations of this infection, (2) consideration of chronic burrowing indolent ulcer in the list of differential diagnoses and (3) adequate and complete bacteriologic studies. Earlier institution of zinc peroxide treatment might have saved this man's limb. Failure to obtain permanent improvement with ordinary measures should serve as the most forceful argument for the urgent need of early diagnosis. Freshly prepared potent zinc peroxide cream when applied to all affected parts of such a wound and protected against drying is dramatic. Within a few days the exudation ceases, granulations start filling in, the undermining becomes less and the wound takes on a healthy appearance. For successful treatment the zinc peroxide cream must reach all parts of the wound and the preparation must be potent.

Lung Abscess.—Sweet offers the following suggestions, based on a study of 125 cases of lung abscess, for improving the therapeutic results: 1. Patients should not be allowed to go without operation longer than four months from the onset of disease. 2. Patients with abscesses who do not show definite regressive changes should be operated on within six to eight weeks after onset; often as soon as they are seen and the diagnosis is confirmed. 3. The interval between the two stages of the operation should not exceed four or five days; in the desperately sick patients, not more than twenty-four or forty-eight hours. 4. The abscesses of the upper lobe which are not too acute should be subjected to primary lobectomy in preference to drainage. 5. Certain abscesses should be drained as a preliminary procedure with the idea of performing a lobectomy at a later date. 6. Redrainage should be abandoned. Patients whose wounds remain unhealed after primary drainage will do better if subjected to lobectomy. The opening of secondary cavities not reached at the first operation is not classified as redrainage. 7. All patients with lung abscess should have the benefit of the combined judgment of the internist, the bronchoscopist, the thoracic surgeon and the roentgenologist. Improved results will probably ensue if the bacteriology and the related problems of immunology in these cases are understood better.

Acute Cholecystitis.—According to Fallis and McClure, the mortality in 320 consecutive operations for acute cholecystitis performed at the Henry Ford Hospital was 5.3 per cent. The maximal preoperative temperature is of some prognostic value. The death rate of patients whose preoperative temperature was above 102 F. was three times that of those whose temperature remained below 102 F. Preoperative pulmonary disease increased the risk of operation three times, and cardiac disease doubled it. The lowest mortality rate was obtained in cases in which operation was delayed for at least seventy-two hours from the onset of acute symptoms. It appears best to delay operation until the fluid balance is restored, the glycogen content of the liver is augmented and an estimate of liver function is made. The highest mortality rate was in the gangrenous cases. Gallstones were present in 90.9 per cent of the patients. A postoperative temperature of above 103 F. is of considerable prognostic value, for the mortality among such patients was 28 per cent. Less than 15 per cent of patients were discharged by the seventeenth postoperative day and more than 20 per cent remained in the hospital longer than thirty days. The short duration of life in the fatal cases—more than 80 per cent of the deaths occurred before the fifth postoperative day—suggests that hepatic insufficiency might be a factor in the mortality.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Children's Diseases, London

37:89-152 (April-June) 1940

Erythroblastic Anemia. F. R. B. Atkinson.—p. 89.
Dyschondroplasia (Ollier) of Upper Limb with Other Developmental Abnormalities. T. Anwyl-Davies and F. P. Weber.—p. 110.
Encephalitis Complicating Whooping Cough with Subsequent Development of Epilepsy. C. Worster-Drought.—p. 115.
Hydrops Foetalis: Case. J. V. O'Sullivan and J. R. Gilmour.—p. 119.

British Medical Journal, London

1:839-878 (May 25) 1940

*Effect of Intrapartum and Neonatal Administration of Synthetic Vitamin K Analogues on Newborn. A. I. S. Macpherson, E. McCallum and W. F. T. Haultain.—p. 839.
Perforated Jejunal Ulcer Following Partial Gastrectomy. W. A. Law.—p. 844.
Use of Thiersch Skin Graft. B. K. Rank.—p. 846.
Barbiturate (Soneryl) Poisoning: Account of Case Showing Value of Picrotoxin in Treatment. G. M. Slot.—p. 849.
Tuberculosis: Case. T. F. Miles and M. Curwen.—p. 850.

Intrapartum and Neonatal Synthetic Vitamin K Administration.—Macpherson and his associates estimated the prothrombin index in fifty-four infants during the first week of life. The principal feature was the extreme variation in the prothrombin index between different individuals on the same day and in the same case on different days. An appreciable decrease from the cord estimation was often demonstrated within twenty-four hours and this fall continued, reaching its lowest value from thirty-six to eighty-four hours post partum. About the fifth day post partum the prothrombin level rose sharply and became stabilized at about 75 per cent. It gradually rose over a period of months. A vitamin K analogue was given in the early neonatal period to thirty-six babies. The administration of 2-methyl-1 : 4-naphthoquinone and diacetyl-2-methyl-1 : 4-naphthohydroquinone to twenty infants within twenty-four hours of birth raised the prothrombin index to from 80 to 90 per cent and stabilized it at that level during the first few days of life. This effect was independent of the cord prothrombin index, of the antenatal condition, of prematurity and of the type and duration of labor. The quinone given orally appeared to be less potent than quinol diacetate. The quinol diacetate corresponded closely in activity to the quinone parenterally. There was no difference in the effects produced by the injection of 2.5 mg. and 5 mg. of the quinone. The unusually rapid action of 2-methyl-1 : 4-naphthoquinone intramuscularly is confirmed by the effects in five cases. In one case an increase from 44 per cent to 63 per cent was noticed in 100 minutes, and in another from 50 per cent to 85 per cent in 150 minutes. Thirty-one mothers were given a vitamin K analogue ante partum. The effect on the prothrombin index of the infant during the first week of life was qualitatively identical with that obtained by giving the same substances directly to the baby during the first twenty-four hours of life. There is no advantage in giving more than 50 mg. by mouth to mothers. The maximal effect will be obtained in the newborn if an adequate dose is given to the mother between twelve and four hours before delivery. The contents of the intestine are sterile in the newborn. Therefore enough vitamin K cannot be absorbed until bacterial invasion of the bowel occurs. Breast feeding or the use of unsterilized breast milk on the first day should assist this synthesis by supplying numerous harmless bacteria, but this does not afford any protection against the fall in plasma prothrombin. Adequate administration of vitamin K analogue to the mother before delivery appears to be the most rational method of treating prothrombin deficiency in the newborn and its administration may become as routine as the use of vitamins A and D earlier in pregnancy. Its administration either to the mother before delivery or to the newborn would appear to be especially indicated (1) in cases of maternal toxemia, (2) in premature labor, (3) in difficult or instrumental delivery, (4) when breast feeding is not possible, (5) when any cerebral symptoms develop during the first few days of life, (6) in cases of hemorrhagic diathesis, icterus gravis neonatorum and anemia and (7) when an operation is necessary on the newborn.

Medical Journal of Australia, Sydney

1:573-608 (April 27) 1940

*Antidiuretic Substance in Urine in Relation to Normal and Toxemic Pregnancy. Vera I. Krieger and T. B. Kilvington.—p. 575.
Recent Advances in Pathology of Blood Transfusion. N. M. Gutteridge.—p. 585.

1:609-650 (May 4) 1940

Pathology in Practice. K. Inglis.—p. 609.
Atelectasis and Pulmonary Tuberculosis. C. Harvey and B. White.—p. 613.
Australian Medical Work in Korea. C. I. McLaren.—p. 624.

Antidiuretic Substance in Urine in Pregnancy.—Krieger and Kilvington examined the urine of ten nonpregnant women, sixteen normal pregnant women, fourteen pregnant women with toxemia and eighteen with eclampsia for the presence of an antidiuretic substance. They describe their method for the preparation of the urinary extracts. Standard volumes of 100 cc. of urine, or protein-free filtrate from urine containing albumin, dialysed and concentrated to 10 cc., were used. The biologic assay of the urine preparations was done according to Burn's method for determining the antidiuretic potency of pituitary extracts. In this method, inhibition of water diuresis can be detected by the comparison of the urinary excretion of four mature male rats injected with preparations from the patient's urine with that of four control rats. Most workers have calculated the magnitude of the antidiuretic activity by measuring the difference in the times required for the volume of urine excreted by the rats injected with urine concentrates to equal half that of the water ingested and for the corresponding volume of urine to be excreted by the control rats. By this method only the time factor is taken into account. The authors emphasize that another method of assessing the antidiuretic potency of a urine concentrate is to determine its total effect by measuring the differences in the areas subtended by the graphs obtained when the total volumes of urine excreted by the control rats and by the treated rats are plotted against the time. In the present investigation both methods were used. The authors found that the method of the measurement of differences in areas shows delayed as well as immediate inhibitory effects and therefore is a more reliable means of estimating antidiuretic activity. Summarizing their results the authors state that a pituitary-like substance inhibiting water diuresis was found in small amounts in concentrates of the urine of some nonpregnant women and frequently in larger amounts in concentrates of the urine of normal pregnant women. Preparations from urine obtained from preeclamptic and eclamptic patients frequently contained large amounts of this antidiuretic hormone. The maximum concentration was observed at the height of toxemia, when albuminuria, oliguria, edema and raised blood pressure were present. With concentrates of 100 cc. samples from successive specimens of urine of patients suffering from eclampsia and preeclampsia, a sharp decrease in antidiuretic potency followed the maximum value and was accompanied by a decrease in edema and an increase in urinary excretion.

1:681-712 (May 18) 1940

Abdominal Pain and Integration of Patient. V. J. Kinsella.—p. 681.
*Modern Clinical Methods to Combat Whooping Cough Infection. S. W. Williams.—p. 690.
Trichomonas Vaginalis Vaginitis and Monilial Vaginitis: Their Diagnosis and Treatment. R. F. Matters.—p. 693.

Methods for Combating Whooping Cough.—Williams points out that of 144 ambulatory patients suffering from mild whooping cough, diagnosed on clinical evidence, 115 (80 per cent) gave positive reactions to cutaneous tests when first tested. Of the twenty-nine children who did not react to the first test, eleven gave a positive response on being retested three weeks later. The other eighteen children did not attend for a second test. These observations suggest that response to the test becomes positive during the progress of the disease. Twelve hospitalized children suffering from severe attacks for from four to thirteen weeks gave no reactions. An opportunity did not arise of testing these children during or after convalescence. Probably the reaction would have become positive. Twenty-nine of eighty-one children attending the Children's Hospital for treatment for diseases other than pertussis had, according to the mothers, a history of whooping cough; ten gave positive reactions to cutaneous tests and nineteen did not. Of fifty-two children whose mothers stated that they had not had whooping cough, forty-seven gave no reaction and five gave positive reactions. There is a statistically significant correlation between a history of clinical whooping cough and a positive response to the cutaneous test. However, the correlation is not absolute. The five children may have suffered from a mild undiagnosed attack of whooping cough. Such attacks undoubtedly occur and can be diagnosed only by bacteriologic methods. Some or all of the nineteen children with histories of whooping cough who did not react to the cutaneous test may not have had whooping cough or the mother's statement may not have been completely reliable. On the other hand, it is not unlikely that the response to the test may change from "positive" to "negative" in a proportion of children within a few months or years after recovery. In the present state of knowledge it is probably safest to immunize all children who have not had whooping cough. By gradually increasing the initial and subsequent dosages of phase I vaccine in different groups of infants the author found it possible to give an initial dose of 7,500 million organisms and four subsequent injections of 20,000 million at weekly intervals. The injection was made into the deltoid muscle and the doses, except the first, were divided, 1 cc. of vaccine being injected into each arm. In about 10 per cent of 250 children the reactions were anorexia, fever (101 F.) and a tender erythematous area at the site of injection. About 30 per cent of infants were given two final doses of 30,000 million organisms to replace three injections of 20,000 each without severe reaction. Whether these 250 infants have been protected against whooping cough cannot be answered yet, as there has been no epidemic in Melbourne. Recent work shows that at least 80 per cent of infants immunized with phase I vaccine are protected against the disease. How long the immunity lasts and whether it is advisable to give a further dose of vaccine one year after the first injections are points still under debate. Until a method of testing a child's immunity, comparable perhaps with the Schick test for diphtheria is had, the control of dosage in whooping cough will be difficult. A ready source of possible antibody for passive immunization is parent's blood; 15 cc. of such blood is injected into each buttock. It is a somewhat painful procedure for the child, but the injected blood is apparently absorbed in twelve hours and no untoward reactions occur. Of fifteen infants treated thus the disease was mild in thirteen and severe in two. A comparison with forty-two controls shows twenty mild cases, eighteen severe and four cases of bronchopneumonia. An early diagnosis is essential for successfully lessening the effect of the disease. A positive cough-plate finding and the presence of a whoop are the only certain means of diagnosis. The former method is the only available one in the early stage of the disease.

Quarterly Journal of Medicine, Oxford

9:129-192 (April) 1940

Nitrogen and Chloride Metabolism in Gastroduodenal Hemorrhage. D. Black and A. Leese.—p. 129.
*Galactose Tolerance as Test of Liver Function. N. F. Maclagan.—p. 151.
*New Observations on Etiology and Prognosis of Achrestic Anemia. M. C. G. Israëls and J. F. Wilkinson.—p. 163.
Aleukemic Leukemia. M. Hynes.—p. 177.

Galactose Tolerance as Test of Hepatic Function.—Maclagan determined the hepatic function by the galactose tolerance test of fifty normal persons (twenty healthy male medical students and thirty outpatients suffering from various diseases unconnected with the liver, thyroid or gastrointestinal tract), six cases of diabetes mellitus, ten of toxic jaundice, six of obstructive jaundice and twelve of exophthalmic goiter. The students gave a slightly lower reading than the normal controls. However, the difference was hardly great enough to be of clinical importance. All the toxic and none of the obstructive cases of jaundice showed impairment of hepatic function. This suggests that the test should be of some value in the differential diagnosis of jaundice. In ten of the twelve cases

of exophthalmic goiter, definite impairment of hepatic function was observed. This was extreme in some cases. These were clinically severe cases, with basal metabolic rates ranging from +20 to +80 per cent (average +55 per cent). This observation is in agreement with the results of Boyce and McFettridge (1938), who used the hippuric acid test. There seems little doubt that this hepatic damage is a part of the pathologic changes of hyperthyroidism, although it has not yet received general recognition. The clinical value of the test depends on its power of testing one function of the liver which is independent of the excretion of bile. This information may be useful for the following purposes: 1. The demonstration of hepatic damage in diseases in which its presence is uncertain or unconfirmed; hyperthyroidism, pneumonia, after surgical operations and rheumatoid arthritis. 2. The detection or confirmation of hepatic cirrhosis. The test is of particular value when jaundice is slight or absent. 3. This is of value for the differential diagnosis of toxic from obstructive jaundice. The pigmentary tests are, in general, unreliable for this purpose. The cases of jaundice studied are too few to reveal the limitations of the test in this respect, but they did fail to show any disagreement with the results expected, as all the toxic and none of the obstructive cases showed impaired function.

Etiology and Prognosis of Achrestic Anemia.—Israëls and Wilkinson present six cases of achrestic anemia in which particular attention was paid to the pathologic changes in the bone marrow. All the patients are still alive. The marrow was studied by sternal biopsy. In all of them there was a true megaloblastic hyperplasia, a hyperchromic megalocytic anemia, free hydrochloric acid in the gastric juice and a variable response to liver therapy. Patients 4, 5 and 6 were young women. The latter group resembles in some respects the so-called pernicious anemia of pregnancy. None of the patients were pregnant, but their response to liver treatment was better than in the cases reported previously, and their progress raises the hope that the prognosis, like that of pernicious anemia of pregnancy, will also be better than that of the previous cases. The present patients are, on the average, younger (58, 42, 27, 20, 17 and 25 respectively) than the former ones but this does not clash with the suggestion that achrestic anemia is allied to pernicious anemia, as the latter disease is now known to occur at an earlier age than was formerly thought. Some workers find difficulties in the differential diagnosis of achrestic anemia. Vaughan (1936) classifies it with megalocytic anemia due to liver disease, but the authors state that the necropsies of their previously reported cases failed to show any lesion in the liver apart from the fatty changes common to all prolonged anemias. The changes in the bone marrow of achrestic anemia often show a mixture of normoblastic and megaloblastic hyperplasia—corresponding to the partial response to liver—which is not like that of pernicious anemia in relapse. If the Price-Jones curve is thought to reflect changes in the marrow, it is not surprising that the curves of achrestic anemia do not at all times resemble those of pernicious anemia in relapse. Dyke and Young (1938) think that achrestic anemia is related to megalocytic hemolytic anemia. In hemolytic anemias the marrow shows an exclusively normoblastic hyperplasia. However, the chief difficulty has been the differentiation of achrestic and aplastic anemias. This confusion apparently has two sources: the association of the classic symptoms of aplastic anemia with a hyperplastic marrow and the nomenclature of the erythroblastic cells. The sternal marrow biopsies now reported confirm the postmortem observations described earlier that the marrow changes in achrestic anemia resemble those of pernicious anemia. Achrestic anemia is due to some interference with the proper action of the anti-pernicious anemia liver principle on the erythropoietic tissues. The correct differentiation of achrestic anemia is important when treatment is considered. First specific anti-pernicious anemia treatment should be given; larger total doses are required than for pernicious anemia, but they should be spread over a long period. As the more highly purified liver extracts may not contain all the active material, it is better to give one of the less highly purified intramuscular extracts. Blood transfusion seems to be necessary for the majority of patients. For young women it may be necessary only to tide over a specially difficult period. This may be contrasted with the treatment for aplastic or hemolytic anemias. Anti-pernicious anemia treatment is not indicated for either of these conditions; repeated transfusions are necessary in aplastic anemia, while in hemolytic anemia transfusion is often followed by a decision for splenectomy. Splenectomy has no place in the treatment of achrestic anemia.

Presse Médicale, Paris

48:465-488 (May 8-11) 1940

New Method of Therapeutic Impaludation. P. Mollaret and J. Schneider.—p. 465.
*Hematuria in Hemophilic Patients. P. Emile-Weil.—p. 468.
Amebic Dysentery in the Army. M. Poirot.—p. 469.
*Treatment of Meningococcic Meningitis with Sulfanilamides. A. Rusesco, V. Voiculesco and A. Diaconu.—p. 471.

Hematuria in Hemophilic Patients.—Emile-Weil reports a case of hemophilic hematogenic hematuria. A man aged 29 had had a large hemarthrosis of the left knee ten years before. He had the present hematuria for eight days with violent right lumbar pains irradiating toward the penis, accompanied by pollakiuria and vomiting. Following transfusion of 200 cc. of blood, the urine became clear in three days without gravel or sand. Blood calcium was normal and calciuria decreased. Roentgenography revealed an oval shadow, undoubtedly a calculus, at the level of the twelfth rib opposite the inferior calix of the left kidney. The patient recovered in two weeks. Hematurias in hemophilic patients are first observed as a rule between the ages of 10 and 30. Such hematurias are caused by latent renal lithiasis preceded by hemarthrosis which is accompanied by a considerable decalcification of the femorotibial epiphyses and other articulations that may be involved. For a stone to form there must be an anomaly of the renal canaliculi causing urinary stasis, in addition to the decalcification of osseous lesions and temporary hypercalciuria at the time of hemarthrosis. One should differentiate between hemophilic or hemophilo-hematogenic hematurias and hematogenic hematurias caused by physiopathologic processes other than lithiasis.

Treatment of Meningococcic Meningitis with Sulfanilamides.—Rusesco and his collaborators treated ten cases of epidemic cerebrospinal meningitis, eight with soluseptazine (a benzyl-sulfanilamide derivation) in a 6 per cent solution and two with serum and azosulfamide in a 2.5 per cent solution. Nine patients recovered and one died. Five were nurslings aged from 2½ to 11 months and the others ranged in age from 2½ to 13 years. The drug was administered intraspinally, intramuscularly and in one instance orally. The disease lasted from two to seven days. The benzyl-sulfanilamide derivative was administered in decreasing doses as the patients' condition improved. Single injections amounted to from 10 to 15 cc. intraspinally and from 10 to 20 cc. intramuscularly in nurslings and approximately the double of this amount in older children. The total dosage of the substance was from 15 to 23 Gm. in nurslings and from 25 to 34 Gm. in the other children. To avoid relapse, prolongation of treatment to fifteen days is advisable. The authors recommend treatment of meningococcic meningitis with sulfanilamides exclusively and suggest combining serotherapy only in case the sulfanilamide is not well tolerated. The study of the literature reveals that the statistics for intraspinal and oral treatment are equally favorable. Intraspinal treatment is advised on account of its rendering possible the immediate concentration of the drug in the cerebrospinal fluid even though of short duration and because in the opinion of some investigators the inflamed meninges have a diminished permeability to sulfanilamides. Oral treatment is advised on account of the rapid elimination of intraspinally injected sulfanilamide and on account of the possible occurrence of meningococcic septicemia and encephalitis. In the presence of renal impermeability, administration into the blood is preferable. Sulfanilamide treatment gives a higher percentage of cures than serotherapy, particularly in nurslings. One should bear in mind that there are different strains of meningococci, some sensitive to sulfanilamides and others to serum. Meningococcus B infection should be treated with sulfanilamide. In the course of sulfanilamide treatment cyanosis, cutaneous eruptions, digestive

upsets and changes in the blood picture may occur. It is wise to examine the blood picture from time to time and check the complications.

48:529-552 (May 22-25) 1940

Food Imbalance (Vitamin A Deficiency) in Relation to Calculus of Urinary Tract. G. Mouriquand, J. Rollet, V. Edel, Pape and H. Tete. —p. 529.

Arsenotherapy in Massive Instillated Doses in Grave Puerperal Infection. A. P. Ramos and A. A. Montes.—p. 530.

*Procaine Hydrochloride Infiltration of Left Stellate Ganglion in Paroxysmal Tachycardia: Case. P. Véran, R. Dubois and Chevrel.—p. 533.

*Sulfanilamide-Treated Human Plasma: Its Advantages in Emergency Transfusions. A. Bécart and B. Philippe.—p. 535.

Paroxysmal Tachycardia.—Véran and his associates report the successful management of a case of paroxysmal tachycardia by procaine hydrochloride infiltration of the left stellate ganglion. The patient, aged 43, in whom the shock of bad news had suddenly induced an attack of tachycardia, rapidly grew worse with increasing dyspnea, anorexia, insomnia, an overpowering feeling of fatigue and extreme motor and mental excitement. Roentgenologic examination revealed enlargement of the heart. Various therapeutic measures, including intravenous injections of quinidine, failed. Procaine hydrochloride (10 cc. in a 1:200 concentration) was injected into the left stellate ganglion thirty-two days after the onset. Within twenty-three hours cardiac action had become normal and all symptoms of cardiac failure gradually disappeared. An electrocardiogram taken seven months later showed cardiac rhythm. The authors present electrocardiographic views taken before and after injection. They believe, however, that the use of procaine hydrochloride is determined not so much by laboratory evidence as by diagnosis based on long existing tachycardia, increased pulse and previous cardiac lesions. The interval of time (twenty-three hours) between the injection and the manifest signs of recovery is not regarded as unusual. They briefly review the six cases previously reported in the literature of the treatment of paroxysmal tachycardia by procaine hydrochloride injected into the stellate ganglion.

Sulfanilamide-Treated Human Plasma.—Bécart and Philippe, correlating their discussion with data obtained by previous investigators, appraised the value of human blood plasma treated with sulfanilamide in comparison with that of total blood and of artificial solutions, in emergency situations such as are created by the war. They described the laboratory technics involved, observed characteristics exhibited by the therapeutic solutions under discussion and stressed the bactericidal and bacteriostatic power of the medicated plasma. Sulfanilamide adds a satisfactory viscosity to the human plasma that is especially effective if injected rhythmically, either intravenously or intramuscularly. Possessing sterile properties, it cannot transmit infection. It requires no "grouping" like total blood and hence is free from agglutination accidents. It is not affected by conditions of temperature and can easily be transported where needed. Its usefulness seems to be enhanced by the observation that it does not deteriorate as rapidly as stored blood. The whole subject requires fuller investigation.

Giornale Ital. di Dermatologia e Sifilologia, Milan

81:197-414 (April) 1940. **Partial Index**

*Histopathology of Gonorrheal Vaginitis in Young Girls: Special Reference to Modifications of Vaginal Mucosa from Estrogen Treatment. P. Pinetti.—p. 325.

Ide's Test for Serodiagnosis of Syphilis. C. Marchi.—p. 343.

Histopathology of Gonorrheal Vaginitis in Young Girls.—Pinetti performed biopsies on the vaginal mucosa of five girls from 3 to 7 years of age suffering from acute gonorrheal vaginitis of one month's duration. Biopsy was performed before, during, at the completion and one month after discontinuation of the treatment, which consisted of hypodermic injections of estrogen up to a total dose which varied between 12,000 and 18,000 international units. Microscopic studies revealed the following alterations of the vaginal mucosa: acute inflammation, degeneration and regression of the epithelial cells, intercellular edema, partial or complete destruction of the epithelium, intraepidermic migration of a large number of polymorphonuclear leukocytes, moderate hyperplasia of the epithelium, edema of the subperithelial connective tissue, diffuse cellular polymorphous infiltration of the tissues, with predominance of plasma cells, moderate hyperplasia of the lymphatic tissue, dilatation of the blood vessels and subepithelial hemorrhages. These alterations regress in the course of estrogen therapy and are replaced by hyperplasia, metaplasia and cornification of the epithelium; the infiltrated tissues regenerate, and plasma cells become rare and lymphocytes numerous. At the completion of the treatment, infiltration of the subepithelial connective tissue has completely disappeared; the vaginal mucosa exhibits epithelial hyperplasia and cornification, which regress in about one month, at which time the vaginal mucosa is normal for the age of the patient.

Lotta Contro la Tubercolosi, Rome

11:67-140 (February) 1940

*Modifications of Results of Serologic Tests for Tuberculosis During Tuberculin Reaction. M. de Marchi.—p. 67.

Early Results of Immunitary Specific Therapy of Exudative Pleurisy with Tuberculous Vaccine. M. Bassi and N. Carinci.—p. 86.

Complement Fixation Tests for Tuberculosis During Tuberculin Reaction.—De Marchi studied the behavior of the reaction of complement fixation, Meinicke and Takata-Ara flocculation reactions and Weltmann's reaction during the various phases of the intradermal tuberculin reaction in 102 cases of pulmonary tuberculosis of different clinical types in the course of a sanatorium regimen or surgical therapy. The tests were done before intradermal inoculation of 0.10 cc. of diagnostic anatuberculin and again twenty-four, forty-eight and seventy-two hours after. The author found that there was no relation between the intensity of the cutaneous reaction and the results, either positive or negative, of the serologic tests, which followed parallel curves during the course and at the end of the tuberculin reaction with early diminution and late increase of the figures in the curves. The Meinicke test is the most sensitive to the influence of tuberculin. Partial changes from positive to negative results of the serologic tests, or vice versa, and total inversion of the results of the four serologic tests in the same case during tuberculin reaction were rare. Such a total inversion of the four tests in the same case took place in only one out of 102 cases. The author concludes that tuberculin introduced in the body of a patient with tuberculosis lowers the immunity and produces changes in the organic reactivity of the type caused by reinfection or exacerbation of tuberculosis. The serologic tests correspond with the development of new foci of tuberculosis, as indicated by diminution of the number of antibodies, imbalance in the ratio of albumins and globulins, lowering of the threshold of heat coagulation of the blood serum and increased velocity of sedimentation of the erythrocytes. The variations in the organic reactivity are transient and disappear when the tuberculin reaction is over. The author points out the importance of carrying out serologic tests for diagnosis and prognosis of tuberculosis at a distance from the intradermal tuberculin test in order to obtain reliable results.

Deutsche Zeitschrift für Chirurgie, Berlin

253:325-434 (March 14) 1940

Criticism of Effect of Chordotomy from Anatomic Point of View: Study of the Spinothalamic Tract. M. Kuru.—p. 325.

Blood Gas Exchange and Quantity of Circulating Blood in Narcosis Induced by Intravenous Administration of N-Methyl-C-C Cyclo-Hexamyl-Methyl Barbituric Acid and C-C-Isopropyl-B-Bromallyl-N-Methyl Malonylureid. E. Derra and J. Korth.—p. 381.

*Roentgenoscopy in Acute Abdominal Disorders. O. Kapel.—p. 399.

*Treatment of Brown Giant Cell Tumors by Implanting Cortical Fragments Derived at Site of Operation. E. Hohlweg.—p. 427.

Roentgenoscopy in Acute Abdominal Disorders.—Kapel reports on the diagnostic value of roentgenoscopy, which he employed with and without contrast mediums in some 400 routine cases of acute abdominal conditions such as ileus, perforations in the gastrointestinal tract, involvement of the urinary tract, invagination, trauma and the presence of foreign bodies. In 120 cases of ileus, about half of which were conservatively managed, x-ray examination confirmed the clinical diagnosis. In several cases clinically unsuspected ileus was promptly discovered. In seven cases of pneumococcic and gonococcic peritonitis with obscure clinical pictures, extensive ileus was found. On the other hand, thirty-five cases of pathologic conditions clinically suspected as ileus because of the presence of the typical signs were roentgenologically found to be cases of pseudo-ileus. In some of these cases intravenous urography disclosed an

obstruction in the urinary tract. In fourteen cases of perforated ulcer, preoperative discovery of air in the peritoneal cavity was considered an indication to prompt surgical intervention. In eleven cases of intussusception, x-ray study with the aid of a contrast medium showed successful disinvagination taking place without recourse to narcosis. The author admits the possibility of roentgenologic error in the diagnosis of ileus involving the colon. He stresses roentgenologic study in the diagnosis of acute renal and ureteral calculus. Hematuria may often be absent from the clinical picture during onset. In 110 cases of obscure abdominal lesions no diagnostic aid was derived from roentgenoscopy.

Treatment of Brown Giant Cell Tumors.—Hohlweg reports five cases of osteitis fibrosa cystica successfully managed by curetting and then implanting small fragments of cortical bone substance derived from the site of the surgical intervention. Spongy bone substance was used only as a supplementary material in larger cavities. The procedure consisted in first fenestrating the bone and thoroughly scraping away all tumor growth. Extensive portions of the bone cysts were then removed, leaving only a shallow trough. Pieces of cortex obtained in the operative act were reduced to the size of a pea and closely packed into the bone hollow. The periosteum was then sutured together over the closely packed bone fragments as far as it could be done and the limb left in a plaster cast for from four to eight weeks. This procedure made unnecessary the invasion of any other part of the skeletal system and seemed to favor more rapid healing. The author briefly reviews the other surgical procedures employed in the treatment of brown giant cell tumors.

Klinische Monatsbl. f. Augenheilkunde, Stuttgart

104:369-472 (April 30) 1940. **Partial Index**

Hemeralopia in Soldiers. K. vom Hofe and M. Glees.—p. 369.
Color Vision in Street Traffic. K. Velhagen.—p. 377.
Relapse of Tuberculous Eye Disease. W. Hallermann.—p. 387.
New Endeavors in Fight Against Tuberculosis of the Eye. W. Wegner.—p. 395.
*Value of Tuberculin Test According to Mantoux in Diagnosing Tuberculous Etiology of an Eye Disease. H. Schlichting.—p. 401.
Subretinal Liquid in Melanosarcoma of Choroid. P. Cibis.—p. 424.

Mantoux Test in Diagnosing Eye Disease.—By intracutaneous injections of human and bovine tuberculin in eighty-seven cases of nontuberculous and eighty-seven cases of possibly tuberculous disease of the eye, Schlichting determined the weakest tuberculin concentration capable of causing a positive reaction. The author observed that (1) there was no essential difference between the human and the bovine tuberculin as to action, (2) the reactions of the two groups did not differ essentially and (3) the majority of tuberculous patients reacted negatively or their reactions became positive only with higher tuberculin concentrations. The author concludes that the Mantoux test is not suited for the diagnosis of the tuberculous etiology of diseases of the eye.

Medizinische Welt, Berlin

14:497-520 (May 18) 1940. **Partial Index**

Conjunctival Disorders: Differential Diagnosis and Treatment in General Practice. R. Braun.—p. 497.
*Question of Epidemiology and Pathogenesis of Acute Pneumonia on Basis of 1,002 Cases. G. Wiele and H. Ibeling.—p. 500.
Psychotic Disturbances in Patients with Decompensated Heart Disease. W. Lueg and R. Weber.—p. 505.
Chediak's Dry Blood Test for Syphilis and the Meinicke Clarification Reaction II. E. Zimmermann.—p. 507.
Role of Urea in Modern Treatment of Wounds. J. Husslein.—p. 508.

Epidemiology and Pathogenesis of Acute Pneumonia.—Increased incidence of acute pneumonia with high mortality induced Wiele and Ibeling to investigate its pathogenesis and epidemiology. Their studies were made on 1,002 patients with acute pneumonia who were admitted to the Krupp Hospitals. The disease was especially frequent among men of the ages between 35 and 45. Morbidity as well as mortality were lower among women and children. Graphic records of the morbidity and mortality rates throughout the different months of the years from 1935 to 1939 inclusive indicate a great increase during the winter months and a low incidence during the summer months. It is suggested that the greater number of sunlight hours and the higher vitamin content of the organism play a part in the defense against the infection and thus are important factors in lowering the incidence during the summer months. Cold with its action on the vascular system causes changes in the blood perfusion of the lung and it is assumed that cold reduces the resistance so that pathogenic micro-organisms can exert their effect. The realization that exposure to cold plays an important part in the pathogenesis of pneumonia suggests certain prophylactic measures. Workers should be warned that it is dangerous to depart from the factory by bicycle or motorcycle immediately after the cleansing shower and if insufficiently clad. Similar carelessness in the course of sports should be warned against. Such exposures to cold often result only indirectly in pneumonia, the direct result being a catarrhal infection. Certain meteorologic changes are accompanied by increased incidence of pneumonia. The infectiousness of pneumonia is rejected by the authors on the basis of their clinical observations. Type determination of the pneumococci from patients of sixty-four different industrial establishments disclosed no evidence of transmission among the patients nor was evidence of infection demonstrable among the physicians or the nursing staff. The fact that a patient had a recurrence of pneumonia of the same type shortly after the first attack speaks against a prolonged immunity after pneumonia.

14:521-544 (May 25) 1940

Accident and War Surgery. M. zur Verth.—p. 521.
Correlation of Incretory Glands. F. Utz.—p. 523.
Desensitization (Rational Bee Venom Therapy) with Apicosan in Rheumatism of Allergic Origin. E. Kirchner.—p. 528.
*Therapy of Hyperemesis Gravidarum in Practice. F. Holldack and Hildegard Holldack.—p. 529.
Results of Examination of Cancer Patients in Nuremberg During the Years from 1933-1934 to 1937-1938. M. Meyer.—p. 531.

Therapy of Hyperemesis Gravidarum.—The Holldacks used a preparation containing vitamin B_1 and a liver extract in the therapy of severe as well as mild cases of hyperemesis gravidarum. The treatment was successful in all nineteen cases in which it was employed. The preparation is available in ampules and the administration is by intragluteal injection. In some of the cases four injections were sufficient, whereas in one case six were necessary to effect complete cessation of the attacks of vomiting. The authors feel that one injection each on three successive days is the best mode of treatment. No other therapeutic measures are necessary in addition to the vitamin B_1 and liver therapy. Many of the women commenced to gain weight shortly after the treatment. The vitamin B_1 and liver therapy was effective also against nausea without vomiting.

Wiener klinische Wochenschrift, Vienna

53:395-414 (May 17) 1940. **Partial Index**

Rare Causes of Sudden Death: Hemorrhage into Abdominal Cavity. H. Winkler.—p. 395.
Spectral Analysis of Eschars. F. X. Mayer and H. Pesta.—p. 397.
Electrocardiographic Examinations on Caisson Workers. W. Breu.—p. 400.
*Serum Prophylaxis in Tetanus. H. von Karnitschnigg.—p. 403.
Question of Race and Colonies. L. Rauter.—p. 405.

Serum Prophylaxis in Tetanus.—Karnitschnigg investigated the problem of serum prophylaxis on the basis of 34,314 injuries. Tetanus antitoxin was administered to 16,269 and was omitted in the treatment of the remaining number. None of the patients who had been subjected to serum treatment developed the disease, while of the other group twenty-nine did. Among these there were twelve fatalities. The effectiveness of excision of the edges of the wound must be rejected. It was not possible in nine (injuries from electric current and extensive excoriations), while in one case tetanus developed in spite of the excision. Serum prophylaxis of tetanus has certain disadvantages, such as the skin eruption with its unpleasant sequels. But in the choice between these complications and tetanus there should be no doubt. The greatly feared anaphylactic shock can be avoided almost entirely if the rules regarding desensitization are followed. Only one case of shock was observed in the reported material. Different serums were used in order to study the disadvantages of the injection of antitoxin. It was found that serum reactions are associated with its protein content and that its reduction may presumably lessen the incidence of the serum disease. The author concludes that serum prophylaxis of tetanus is an essential part of modern wound therapy and that he would not dispense with it under any circumstances.

Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

80:1119-1180 (April 30) 1940

Investigations on Rickettsial Diseases in Sumatra: Pathologic Anatomy of Mite Fever in Human Subjects. W. Kouwenaar.—p. 1119.
Influence of Staying in Cool Temperatures on Oxygen Saturation of Venous Blood and on Minute Volume in Persons Living in Tropics. W. Radsma and Go Giok Khoen.—p. 1140.
*Arakawa's Reaction. D. P. R. Keizer.—p. 1152.
Papillomatous Hypertrophy of Tonsils. J. Kuilman.—p. 1156.
Cylindroma of Upper Eyelid Probably Originating in Tear Gland. J. M. Lebeau-Manders.—p. 1159.
Poisoning by Bite of Sea Snakes. A. Fossen.—p. 1164.

Arakawa's Reaction and Maternal Beriberi.—According to Keizer, Arakawa demonstrated in 1930 a relationship between the peroxidase content of breast milk and the vitamin B_1 content of the maternal organism. Arakawa's test demonstrates whether peroxidase is present in adequate amounts. If the test is positive the blue color appears at once or within one minute; if the peroxidase content is extremely low, the time required is much longer or there is no coloration at all. In order to determine whether beriberi influences the peroxidase content of the milk, Keizer made tests on sixty-two nursing mothers. In nineteen the reactions were positive, in forty-three they were negative. Clinical observations indicated that thirty-two of the sixty-two women were free from beriberi but that thirty were not. Of the thirty-two women who had no clinical signs of beriberi, eighteen had a positive and fourteen a negative Arakawa reaction. Of the thirty with beriberi, one had a positive and twenty-nine a negative reaction. Nine of the thirty women with a history of or with clinical signs of beriberi had nurslings with noticeable signs of beriberi. The author instituted treatment with large doses of vitamin B_1 in women with a negative Arakawa reaction. He reached the conclusion that a positive Arakawa reaction excludes maternal beriberi; a negative one, although not always actually indicating maternal beriberi, can be changed into a positive reaction by the administration of large doses of vitamin B_1.

Acta Medica Scandinavica, Stockholm

104:235-426 (May) 1940. **Partial Index**

Studies on the Causation of Experimental Gastroprival Pellagra: Therapeutic Experiment (II) with Preventive Parenteral Administration of Vitamin B_1, Riboflavin and Vitamin A, Separately and in the Combination Vitamin B_1+Vitamin A. S. Petri, F. Nørgaard and E. Bandier.—p. 245.
Pathogenesis of Bundle Branch Block and Other Preponderance Curves: On False and True Infarction Curves in Precordial Leads. V. Mortensen.—p. 267.
A Method for Quantitative Determination of Prothrombin in Plasma. O. Thordarson.—p. 291.
Cyanosis in Treatment with Sulfonamide Compounds. N. Svartz and S. Kallner.—p. 309.
*On Irreversible Functional Disturbances in Chronic Pellagra. F. Mainzer and M. Krause.—p. 321.
Indications for Operation in Cases of Gastric Disease. D. C. Balfour.—p. 337.
Sarcoidosis (Boeck), Lymphogranulomatosis Benigna (Schaumann); Observations on the Bone Marrow Obtained by Sternal Puncture. S. P. Lucia and P. M. Aggeler.—p. 351.
The Treatment of Schaumann's Disease with Intravenous Injections of a Lipoid-Containing Substance Extracted from Tubercle Bacilli, Possessing the Properties of Tuberculin: A Report of Two Cases. K. Hedén.—p. 386.

Functional Disturbances in Chronic Pellagra.—Mainzer and Krause define chronic pellagra as that stage of the disease in which the skin has reached the phase of hyperkeratosis, evidenced by dry or moist eczema, with or without pathologic pigmentation. The acute disorder occasionally disappears without treatment. The chronic type of pellagra cannot always be cured, even if the patient tolerates a high caloric diet rich in pellagra preventive factor. At a certain stage the pathologic changes probably become irreversible. Moreover, such patients have a marked tendency toward relapse, sometimes depending on and sometimes without relation to the diet. Some investigators interpreted this as an indication that pellagra is not an avitaminotic condition. Although starting from an entirely different point of view, the authors have reached conclusions of importance to this problem. In previous reports they demonstrated that small amounts of insulin (5 units) regularly cause a marked and prolonged lowering of the blood sugar level, frequently accompanied by severe clinical symptoms. This phenomenon was attributed to a functional disturbance of the adrenals. The present report extends and confirms the previous observations. The authors demonstrate that hypersensitiveness to insulin of patients suffering from chronic pellagra persists independently of clinical improvement or cure of the disorder, whereas in acute pellagra clinical cure is apparently accompanied by a complete normalization of the insulin-blood sugar curve. They believe that sooner or later pellagra produces irreversible changes. In this case the clinical cure is nothing but a remission; the relapse represents an exacerbation. The authors think that these observations are important with reference both to the pathology of pellagra and to vitamin research.

Acta Pædiatrica, Stockholm

27:279-401 (May 1) 1940

*Adrenal Hypertrophy in Infants: New Clinical Entity of Neonatal Period. R. K. Dijkhuizen and E. Behr.—p. 279.
*Investigations on Congenital Stenosis of the Pylorus: Its Treatment and Prognosis; Report of 107 Cases Reexamined from One to Twenty-Two Years After Treatment. R. Rinvik.—p. 296.
Roentgenologic Follow-Up Examination in Congenital Pyloric Stenosis After Manifest Stage. K. Andresen.—p. 334.
Poliomyelitis and the Meteorologic Environment. W. F. Petersen and A. Mayne.—p. 353.
Investigations on Growth of Children in Elementary Schools of Finland. A. Ruotsalainen.—p. 374.
Antituberculous Immunity Produced by BCG Vaccine. J. Zeyland and E. Piasecka-Zeyland.—p. 393.

Adrenal Hypertrophy in Infants.—Dijkhuizen and Behr relate histories of four infants presenting symptoms suggestive of intestinal obstruction. In the first, laparotomy failed to disclose an obstruction, and in the other three necropsy excluded intestinal obstruction, but it revealed a striking feature; namely, extremely large adrenals. Although in the first case necropsy was refused, it seems probable that it was also one of adrenal hyperplasia. This child had a perineal hypospadia and evidence of pseudohermaphroditism suggestive of adrenal hyperplasia. A few similar cases of adrenal hypertrophy have been recorded in the literature, and these children were also found to have suffered from intestinal disorders. Most of the patients were boys or pseudohermaphrodites. It is suggested that an increased activity of the cortical hormone was present in these cases. Further clinical, pathologic and experimental data are required to define and explain this new clinical entity of the neonatal period.

Congenital Stenosis of Pylorus: Treatment and Prognosis.—Rinvik reports investigations on 137 cases of congenital pyloric stenosis treated in the department of pediatrics of the State University in Oslo, Norway. One hundred and eighteen of the patients were male and nineteen female infants. Seventy-two patients were treated conservatively. If the three children who were moribund on admission and a fourth who died from a complicating cystopyelonephritis are disregarded, the conservative treatment had a mortality rate of 2.9 per cent (two fatal cases out of sixty-eight). The author points out that before 1933 the therapy was largely surgical, but since the introduction of eumydrine (atropine methylnitrate) there has been a considerable advance in medical treatment. In a total of forty patients who have been treated with eumydrine, recurrence has been observed twice. The average duration of hospitalization for patients treated conservatively has been reduced from eighty-nine to thirty-six days. Signs of intoxication following the administration of eumydrine are rare. Sixty-five patients were treated surgically; the mortality was 7.6 per cent (five fatal cases). The late prognosis has been evaluated on the basis of a follow-up from one to twenty-two years after treatment. Ninety-five patients were reexamined. It was found that there exists a certain amount of familial predisposition to pyloric stenosis in small infants (in ten of 107). The infants do not seem to have a neuropathic disposition as they grow up, but relatively often they suffer from enuresis. They have a certain predisposition to what is termed "constitutional diseases." The defective growth of infants with pyloric stenosis is soon regained, probably within the first year of life. The relationship between weight and height follows the average for normal infants. The x-ray examination showed changes in more than half of the cases, but these were not accompanied by changes in the gastric chemism and they may exist without subjective symptoms.